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A HUGE HEMANGIOMA OF THE LIVER ASSOCIATED WITH HEMANGIOMATA OF THE SKULL AND BILATERAL CYSTIC ADRENALS.

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Hemangiomata of the liver are by no means rare tumors and are probably the most common and best known of all new growths in this organ. In the majority of cases these tumors are small, cause no clinical symptoms and are discovered first at autopsy. The following case, however, seems worthy of record because of the immense size of the hemangioma, its clinical course and its association with similar tumors of the skull and an unusual condition in both adrenals.

Case History.—The patient, A. R., a man, aged thirty-four years, entered St. Margaret's Hospital, service of Dr. P. T. Bohan, on February 15, 1915, complaining of swelling of the abdomen. He had been apparently in perfect health until the age of eighteen, when he noticed that his abdomen was somewhat increased in size. During the past fourteen years it has continued to enlarge until upon admission it had reached the size shown in Fig. 1. He also states the interesting fact that a nephew, aged seven years, has a similar enlargement of the abdomen.

Physical examination showed a large irregular mass in the abdomen, with marked ascites and edema of the ankles. The blood examination showed red blood cells, 3,200,000; white blood cells, 4500; hemoglobin, 52 per cent. (Sahli); Wassermann, negative. The urine contained a trace of albumin and a few granular and epithelial casts.

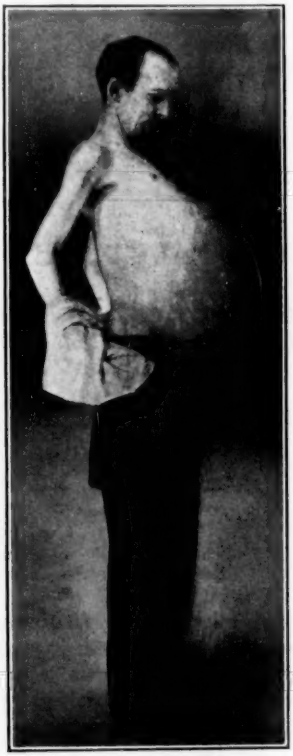

FIG. 1.—Patient on admission.

The patient was under observation for over two years. During this time the blood and urinary findings remained fairly constant. The ascites increased, which made a possible enlargement of the mass difficult to determine. No jaundice developed. The patient died on September 11, 1917, and the autopsy was performed five hours after death. Two hours before the autopsy the body was injected with embalming fluid through the femoral veins.

Autopsy showed the most interesting findings to be in the liver, the skull and the adrenals. Each of these will be subsequently

discussed in order and the results of the macroscopic and microscopic examinations considered. In addition to these findings the body showed an ascites, atelectasis of the lower lobes of both lungs and granular kidneys. The heart, spleen, stomach, pancreas, intestines and bladder showed nothing specially abnormal.

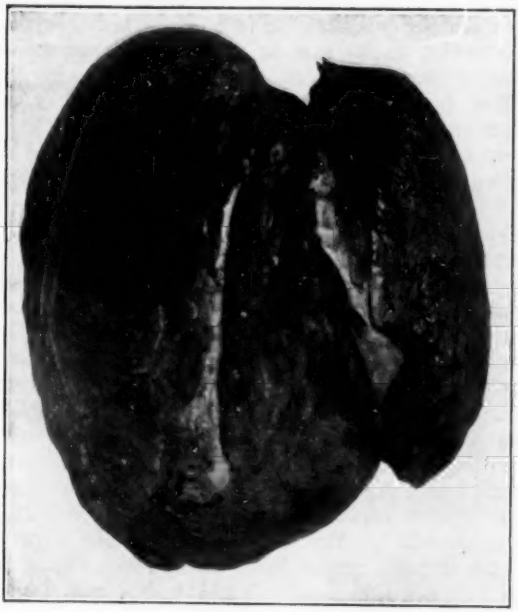

FIG. 2.—Liver of patient.

THE LIVER. The liver (Fig. 2) was greatly enlarged and extended 40 cm. below the xiphoid process of the sternum in the midline. It measured 35 x 44 x 11 cm. and weighed 18,160 grams. The organ was of a dark reddish-purple color, the surface was uneven, somewhat nodular, and the capsule was covered in places with a thick deposit of fibrin. On cut section most of the liver tissue was replaced by a spongy network, in the interstices of which was clotted blood. Here and there were numerous small areas of whitish tissue scattered about which apparently were the remnants of the liver tissue. These areas of liver tissue were largest in the left lobe, where one area measuring 9 x 10 cm. was noted. Throughout the rest of the liver these areas were much smaller, varying from 1 mm. to 2 cm. in diameter, and the hemangiomatous involvement was so extensive that it was often necessary to study the cut

surface very closely in order to make out the remnants of liver tissue. The diagnosis of an extensive hemangiomatous process in the liver was apparent from the naked-eye examination.

The size and extent of the hemangioma make the specimen one of considerable interest. In the majority of cases these tumors are not of sufficient size to produce any general enlargement of the liver or cause any symptoms. Virchow[1] stated in his classic lectures on hemangioma that "as large as the tumor becomes there results, however, no increase in volume of the liver, since the destruction of liver tissue keeps pace with the growing angioma." The largest hemangioma he described measured 3.5 x 4 cm. Schmieden[2] studied 32 cases of hemangioma of the liver, all of which were accidental findings at autopsy and produced no symptoms during life. There are, however, certain cases reported in which the tumor reached a considerable size. Payne[3] reported a case in which the liver showed numerous hemangiomata and weighed 2700 grams (6 pounds).

Langhans[4] described a case of hemangioma of the liver associated with a similar tumor of the spleen. The liver in his case measured 30 x 30 x 18 cm. and was roughly three or four times the normal size. Von Eiselsberg[5] removed a hemangioma of the liver which weighed 470 grams. Birch-Hirschfeld[6] saw a patient in whom the liver hemangioma was so large that the abdomen resembled that of a pregnant woman.

Pfannenstiel[7] operated upon a patient and removed a liver hemangioma weighing approximately 5290 grams (12 Pfund). Langer[8] extirpated a similar tumor which measured 21 x 21 x 11 cm. and weighed 5000 grams Fillipini[9] described a hemangioma of the liver the size of a human head. In Mantle's[10] case the tumor measured 30 x 16 x 4 cm. (12 x 6½ x 1½ inches) and involved the greater part of the right lobe of the liver. Von Genersich[11] saw a tumor as large as a child's head. Chiari[12] described one as large

[1] Die Krankhaften Geschwülste, Berlin, 1863, Bd. iii, p. 393.

[2] Ueber den Bau und die Genese der Lebercavernome, Arch. f. path. Anat., 1900, clxi, 373.

[3] Vascular Tumors of the Liver, Suprarenal Capsules and Other Organs, Tr. Path. Soc., London, 1869, xx, 203.

[4] Casuistische Beiträge zur Lehre von den Gefässgeschwülsten, Arch. f. path. Anat., 1879, lxxv, 273.

[5] Quoted by Langer.[8]

[6] Lehrbuch der pathologischen Anatomie, 1895, Band ii, Heft 2, p. 739.

[7] Erfolgreiche Extirpation eines grossen cavernosen Leberangioms, Allg. med. Centr. Ztg., 1898, lxvi, 1.

[8] Erfolgreiche Extirpation eines grossen Hemangioms der Leber, Arch. f. klin. Chir., 1901, lxiv, 630.

[9] Resection of the Liver, British Med. Jour., 1901, II Epitome of Current Medical Literature, p. 22.

[10] An Unusually Large Angioma of the Liver, British Med. Jour., 1903, i, 365.

[11] Operierter Fall eines kindskopfgrossen Angioma Cavernösum hepatis, Med. Klin., 1908, iv, ii, 1722.

[12] Tumor cavernosus, München. med. Wchnschr., 1909, lvi, 1615.

as a man's head. Roggenbau[13] studied a huge hemangioma of the liver measuring 22 x 9 x 33 cm. This case is apparently the same as that reported by Chiari. M'Weeney[14] reported a case in which the liver was much enlarged, weighing 5100 grams (180 ounces) and the entire left lobe was transformed into an angiomatous mass measuring 25 x 25 x 10 cm. MacCallum[15] mentioned a huge hemangioma of the liver which hung by a stalk from the right lobe and measured 24 cm. in diameter.

These are the largest hemangiomata of the liver that we have found in the literature. In none of these cases was the tumor as large as in our case. Our specimen had produced such an enlargement of the liver that it weighed ten times the normal weight and constituted nearly one-half (4.9) of the patient's entire weight.

FIG. 3.—Microscopic picture of a liver tumor. Zeiss obj. AA, oc. 4.

The microscopic examination of the liver tumor presented interesting pictures which varied somewhat in different parts of the tumor. A common picture (Fig. 3) was that of large dilated spaces filled with blood lying against collections of liver cells, which were often compressed and showed definite evidences of fatty degeneration. In some parts of the tumor small lobules of the liver were surrounded by a dense overgrowth of connective tissue, which

[13] Zur Kenntnis der cavernösen Angiome der Leber, Beitr. z. path. Anat., 1910, xlix, 313.

[14] Enormous Angioma of the Liver, Jour. Path. and Bacteriol., 1911–12, xvi, 401.

[15] A Text-book of Pathology, Philadelphia, 1917, p. 901.

produced a picture suggesting strongly the earlier stages of a cirrhosis of the liver. The connective tissue in such pictures showed marked evidences of proliferation. There were very numerous fibroblasts present and in addition many sprouting and newly formed capillaries of various sizes. These young capillaries varied in appearance from solid tubes of cells to capillaries of increased lumen, some of which showed a degree of distention similar to the cavernous bloodvessels so characteristic of hemangiomata.

In the majority of the section examined the microscopic picture which predominated was that of the large cavernous spaces, with, as a rule, little liver tissue present. The walls of these spaces were formed by endothelium supported by a framework of connective tissue and smooth muscle. Here also there were definite evidences of growth, fibroblasts were numerous and there were many new sprouts sent out from the walls.

Ever since Virchow's studies upon hemangiomata there has been an active discussion as to the genesis and mode of growth of these tumors in the liver. It is beyond the limits of this paper to discuss these various views in any great detail. A brief summary, however, may prove of some interest.

Virchow[16] stated that "the process begins with an increase of the connective tissue of the liver, which is very soon followed by a disappearance of the secretory parts of the organ. In the young connective tissue the vessels dilate and their walls become thickened and fuse with the surrounding connective tissue." This view, that the development of these tumors is caused primarily by a new growth of connective tissue, was also shared by Rindfleisch[17] and by Burckhard,[18] who also mention as important the accompanying "cavernous metamorphosis of the bloodvessels."

Multiple hemorrhages in the liver have been regarded by some as the starting-point in the development of hemangiomata of the liver, while Scheffen[19] considered a passive venous congestion of the liver could produce in time a dilatation of the bloodvessels into cavernous spaces. Beneke[20] described a liver in which a congestion of bile had produced a dilatation of the bile capillaries and compression of the liver cells. He considered the picture to be that of a beginning liver cavernoma.

Ribbert[21] considers hemangiomata of the liver as true new growths which arise from misplacement of tissue and vascular areas

[16] Loc. cit.

[17] Lehrbuch der pathologischen Gewebelehre, 1886, VI Aufl., p. 504.

[18] Beitr. zur pathologischen Anatomie des cavernosen Angioms der Leber, Inaugural Dissertation, Würzburg, 1894.

[19] Beitr. zur Histogenese der Lebercavernome, Inaugural Dissertation, Bonn, 1897 (quoted by Schmieden[2]).

[20] Zur Genese der Leberangiome, Arch. f. path. Anat., 1890, cxix, 76.

[21] Ueber Bau Wachstum und Genese der Angiome nebst Bemerkungen über Cystenbildung, Arch. f. path. Anat., 1898, cli, 381.

in the liver as the result of a developmental disturbance. Schmieden[22] states that cavernoma of the liver are caused by a local transposition of liver tissue which later develops into a tumor-like growth. A growth, however, like that of a genuine bloodvessel tumor does not occur according to his views.

The views of Ribbert and Schmieden have found the greatest number of adherents. Borst[23] states that the cause of most liver hemangiomata is to be found in an embryonal misplacement of liver tissue and that a new growth of bloodvessels cannot usually be demonstrated. For this type of tumor he prefers the name "hamartoma," introduced by Albrecht. However, he adds that "it must be admitted that genuine cavernous 'angioblastomata' of the liver do occur, but they are rarely found. In these cases one finds evidences of growth in the form of endothelial sprouts and tubes." Roggenbau[24] accepts the views of Borst, but has, however, reported careful studies of 2 cases of cavernous angioma of the liver which were examples of genuine new growths.

In our case the evidence is strong that we are dealing with an example of a genuine cavernous angioblastoma in the sense of Borst. The microscopic picture of forming and newly formed capillaries in the young connective tissue between liver lobules indicates active growth, as do the endothelial sprouts which are growing out from the walls of the larger blood sinuses. The gross picture of the liver with such a large amount of the liver parenchyma replaced by cavernous blood spaces is strongly suggestive of an invasive growth, and the suggestion that this process of invasion has been gradual finds support in the clinical picture of a slowly enlarging liver.

In several places the remnants of liver tissue were stained deeply with bile, and these areas were examined carefully to see if pictures could be seen which would substantiate the view of Beneke[25] that a congestion of bile plays a role in the formation of hemangiomata. In these bile-stained areas there were many compressed bile capillaries and ducts and others very widely dilated. The dilated bile ducts were often as large as some of the smaller cavernous spaces, but they contained no blood, and no evidence was found that they formed such blood spaces.

THE SKULL. The next autopsy findings of interest were the changes in the skull. The patient had two prominences: one over the left eye, measuring 3 x 4 cm. in diameter, and another over the right temple, measuring 2 x 3 cm. in diameter. These two prominences were apparently firmly attached to the skull and were as hard as bone. On stripping down the scalp over the right

[22] Loc. cit.

[23] Echte Geschwülste (Blastome) in Aschoff's pathologische Anatomie, 1911, II Aufl., p. 671.

[24] Loc. cit.

[25] Loc. cit.

temple a piece of the temporal bone, including the elevated area, was removed for study.

Examination of the fragment of temporal bone showed that the swelling was produced by a thickening of the bone at that place. This thickening, however, was largely due to an unusually spongy condition of the bone, and with the naked eye large spaces filled with blood could be seen. The microscopic picture showed numerous large blood spaces filled with blood. In some places these spaces lay directly upon the bone, in other places they gave the appearance of dilated bloodvessels coursing in the bone-marrow. Another picture also frequently noted was the presence of large dilated blood-

FIG. 4.—Microscopic picture of a tumor of the skull. Zeiss obj. A2, oc. 4.

vessels surrounded by fibrous tissue, which in turn was lying upon the bone. This picture seems analogous to that in the liver, where the cavernous blood spaces show a markedly developed connective-tissue framework lying against the liver cells (Fig. 4).

The association of hemangiomata of the liver, with similar tumors in other organs, has often been noted. Payne[26] described a hemangioma of the liver associated with angiomata of the adrenals, ovaries and uterus. In Langhans's case[27] the hemangiomata were in the liver and spleen, and Roggenbau[28] describes the asso-

[26] Loc. cit. [27] Loc. cit. [28] Loc. cit.

ciation of a liver hemangioma with a hemangioma of the scrotum. Ullmann[29] has reported a case of liver hemangioma associated with numerous cavernoma of the skin and von Falkowski[30] has studied an interesting case which showed multiple bloodvessel tumors, "mesenchymal Hamartome," in the liver, spleen and skin.

Hemangiomata of the bone are uncommon tumors. Virchow[31] described a case of hemangioma of the parietal bone associated with a liver hemangioma. Schöne[32] has collected 20 cases, 7 of which were of the skull. Von Bruchanow[33] has described a case of cavernous angiomata of the liver, the skin and the periosteum of two ribs. Stamm[34] studied a case which presented hemangiomata in the muscles, bones, cartilage, kidneys, ovaries, small intestine, vocal cords, lungs, skull and brain. No tumors of the liver occurred in his case.

THE ADRENALS. Both adrenals were very much enlarged, of about equal size, measured 11 x 8 x 4 cm., and weighed together 350 grams. The surface was very uneven, numerous cyst-like structures were evident and here and there extensive hard, gritty areas. On puncture of these cysts a thin yellowish fluid escapes after hardening in 5 per cent. formalin. The adrenals cut with much difficulty, and on cut section (Fig. 5) there were numerous cysts present, very irregular in shape and varying in size from 5 cm. to 5 mm. in diameter. Some of these cysts were filled with a clear yellowish jelly-like material while others contained shrunken masses of dark reddish material, apparently clotted blood. In many places the walls of the cysts and the tissue between the cysts contained areas of hard, stony-like substance. These areas of calcareous material were so extensive that it was necessary to decalcify the bits of adrenal tissue that were embedded and sectioned for microscopic study.

Microscopic slides were prepared from different portions of the adrenals, frozen sections and paraffin sections being used for study. The sections were stained with hematoxylin and eosin, Van Giesen's stain and Mallory's anilin-blue stain.

The microscopic picture (Fig. 6) of the larger cysts showed the walls to be composed of a rather dense fibrous tissue, below which were areas of persistent adrenal tissue, the collections of adrenal cells

[29] Multiple Kavernome der Haut und der inneren Organe bei einer Frau. K. K. Gesellschaft d. Aerzte in Wien (quoted by v. Falkowski[30]).

[30] Ueber eigenartige mesenchymale Hamartome in Leber und Milz neben multiplen eruptinen Angiomen der Haut bei einem Saugling, Beitr. z. path. Anat. u. z. allg. Path., 1914, lvii, 385.

[31] Loc. cit., p. 372.

[32] Ueber einen Fall von myelogenen Hemangioma des Os Occipitale, Beitr. z. path. Anat. u. z. allg. Path., 1905, VII, Supplement, p. 685.

[33] Hemangiome der Leber, Ztschr. f. Heilkunde, 1899, xx (quoted by v. Falkowski[30]).

[34] Beitr. zur Lehre von Gefässgeschwülsten, Inaugural Dissertation, Göttengen, 1891 (quoted by Falkowski[30]).

FIG. 5.—Right adrenal with right kidney. Adrenal sectioned in half.

FIG. 6.—Section of adrenal cyst showing wall of cyst, also scattered collection of adrenal cells.

being pushed apart by a dilatation of the capillaries, but still staining intensely. The larger cysts, as a rule, were filled with a rather homogeneous hyalin material staining red with hematoxylin and eosin and yellow with Van Giesen's stain. Some of these masses, however, were not so homogeneous but were granular, and many of them were composed of masses of clumped red blood cells in various stages of disintegration.

FIG. 7.—Section of adrenal showing marked dilatation of the spaces between the adrenal cells.

The microscopic picture of the tissue nearer the center (Fig. 7) showed marked dilatation of the spaces between the columns of adrenal cells. The dilatation varied from what could be interpreted as a simple dilatation of the capillaries or bloodvessels (so-called "sinusoids") to a dilatation sufficient to produce cysts smaller but similar in structure to the large ones. Some of the dilated spaces were filled with blood cells, some contained few red blood cells and others were apparently empty.

The areas of calcification were very extensive. In many places these areas were in the tissue between the cysts, in other places the cyst contents consisted of calcified material and in a few places there were definite patches of osseous tissue, with typical lacunæ and bone corpuscles.

True cysts of the adrenal are unusual. Oberndorfer[35] studied a case of multiple cysts in one adrenal. His specimen showed multiple lymphangiectasis of the adrenal with the formation of smaller and larger cavities and cysts. He also noted marked dilatation of the blood lymph vessels and believed a "stasis of these vessels to be the primary cause, with a resultant cystic degeneration." Sick[36] described a cystic adrenal formed by dilated lymph spaces in which growing lymph capillaries were present. Marchetti[37] studied a cystic adrenal which contained two large cysts and several smaller ones and was interpreted as a degenerative process due to abnormal secretion of the adrenal combined with destruction of the cellular elements. Henschen[38] described under the term "struma suprarenalis cystica hemorrhagica" a single large cyst of the adrenal containing 4000 c.c. of chocolate-brown fluid. He proposes a classification of adrenal cysts into parasitic cysts, false cysts (cystoide) and genuine cysts (cystome). A further subdivision of true cysts he makes as follows:

Cystome:
- (*a*) Epithelial:
  - Follicular.
  - Ciliated.
- (*b*) Endothelial:
  - Lymphangiectasis.
  - Lymphangioma.

Sick's[39] remarkable case of a ciliated cyst of the adrenal is the only case he found belonging to the group of ciliated epithelial cystomata. This condition he considered to be probably due to a developmental displacement of tissue from the urogenital anlage.

McCosh[40] removed a large cyst which was diagnosed as an endothelioma. Doran[41] removed a large single cyst and collected 12 cases of adrenal cysts from the literature, without, however, attempting any classification of them. His specimen showed no minute cysts or lacunæ on cut section. De Vecchi,[42] in 1910, reported what is apparently the first case of bilateral adrenal cysts recorded. He considered his case an example of a lymphangioma. His article contains a very comprehensive study of the literature on

[35] Lymphcysten der Nebenniere, Beitr. z. path. Anat. u. z. allg. Path., 1901, xxix, 516.
[36] Ueber Lymphangiome, Arch. f. path. Anat., 1903, clxxii, 459.
[37] Ueber eine Degenerationscyste der Nebenniere mit kompensatorischer Hypertrophie, Arch. f. path. Anat., 1903, clxxii, 472.
[38] Ueber struma suprerenalis cystica hemorrhagica, Beitr. z. klin. Chir., 1906, xlix, 217.
[39] Flimmerepithelcysten in der Nebennierenkapsel und in einer Beckenlymph drüse, Arch. f. path. Anat., 1903, clxxii, 468.
[40] Cysts of the Suprarenal Gland, Ann. Surg., 1907, xlv, 878.
[41] Cystic Tumor of the Suprarenal Body Successfully Removed by Operation, British Med. Jour., 1908, i, 1558.
[42] Ueber einen Fall doppelseitiger Nebennierenzysten, Arch. f. path. Anat., 1910, cc, 151.

this subject. Nowicki[43] also described a case of bilateral adrenal cysts which he regarded as lymphangiomatous in origin.

Küttner[44] described a large hemorrhagic cyst of the adrenal and collected 12 other cases from the literature. Preusse[45] reported a large lymph cyst associated with amyloid degeneration. He found evidences of proliferation of the lymph vessels and considered his case as a true example of a lymphangiomatous process.

Our case is apparently an example of the group designated by Henschen[46] as true cysts, and its appearance both grossly and microscopically resembles closely the cases considered by their authors as lymphangiomatous. The relative rarity of this condition is indicated by the figures of de Vecchi, who collected, including his own, only 9 cases from the literature, and some of them were doubtful. Nowicki added another case and Preusse reported the eleventh case. Our case is apparently the third case of bilateral cystic adrenals which has been described.

The interpretation of these cases is not altogether clear, as a review of the literature indicates. Nor are the results of the microscopic study of our case altogether satisfactory. The differences between parasitic cysts, false cysts and true cysts are sufficiently apparent, but the distinction between the epithelial and endothelial cysts in the sense of Henschen are not so clear. Some of the descriptions of the epithelial cysts resemble very closely the picture described by other observers as characteristic of the endothelial (lymph) cysts.

Furthermore, the work of Stoerk[47] casts some doubt upon the interpretation of the so-called epithelial cysts. This observer has shown that the adrenal cells form no true acini, with a central lumen which could form a "follicular" cyst as the result of distention by the secretion from the cells. In addition, the idea of an increased secretion from the cells accumulating in the center of the acini runs counter to the generally accepted view that the adrenal cells secrete into the blood stream. Nowicki[48] has substantiated the work of Stoerk.

Most of the observers who have reported lymph cysts of the adrenal have laid much stress upon the dilated spaces which are present between the columns of adrenal cells and also specially marked in the medulla of the organ. These dilated spaces have been generally interpreted as dilated lymph vessels and the process labelled lymphangiomatous.

[43] Zur Kenntnis der Nebennierenzysten, Arch. f. path. Anat., 1912, ccvii, 338.

[44] Beitr. zur Kenntnis und Operation der Struma suprarenalis cystica hemorrhagica, Beitr. z. klin. Chir., 1913, lxxxii, 291.

[45] Ueber ein Lymphangiom einer Amyloid entarteten Nebenniere, Centralbl. f. allg. Path. u. path. Anat., 1914, xxv, 961.

[46] Loc. cit.

[47] Beitr. zur normalen Histologie der Nebennierenrinde, Berl. klin. Wchnschr., 1908, lv, 773.

[48] Loc. cit.

These dilatations, however, as enlargement of structures normally present, would necessitate for their proper interpretation an intensive study of the normal architecture of the adrenal.

Moers[49] and Joesten[50] noted in the medulla large spaces, with connective-tissue walls which were often filled with coagulated fluid. The former considered them lymph sinuses while the latter thought they perhaps had some relation to the lymphatic system. Flint,[51] however, in his classic work on the adrenal, showed by injection methods that these spaces are part of the venous tree, and states that "the large lymphatic spaces described by Moers and Joesten are undoubtedly thin sections of uninjected branches of the venous tree." Also, he found that anastomoses between the veins of the medulla were uncommon and so the previously described venous plexus and sinusoids "must be regarded as a misinterpretation of the venous tree." These observations of Flint indicated clearly that all such spaces cannot at least be interpreted offhand as lymph spaces or that a dilatation of them indicates a lymphangiomatous process. That lymphatic spaces are present to some extent between the adrenal strands seems, however, to be definitely established by the injection experiments of Stilling,[52] who also demonstrated a lymphatic net on the cortex.

In all of the sections of the adrenals in our case the degenerative changes were very striking. The fibrous tissue which formed the walls of the larger cysts showed no lining of endothelium and all presented many large irregular areas of hyaline degeneration and calcification. In many places the only tissue between the large cysts was a rather loose fibrous-like tissue which, however, showed irregular lacunæ apparently produced by softening. When stained with Mallory's anilin-blue stain this tissue stained blue, showing rather numerous strands here and there of connective tissue, which took an intense red stain. In many places also the adrenal tissue showed marked evidences of degeneration, masses of adrenal cells were in varying stages of disintegration, and these masses often had disintegrated to such an extent that there was little left but the framework of reticulum. In places where small groups of cells had perished there were small cysts formed, in other places cysts of considerable size were formed in a similar manner and in many of them fine strands of reticulum were still visible running out from the wall of the cyst toward the center but dissolving before a bridge was formed across the cyst.

The interpretation of these sections, especially in the light of their origin, is a difficult matter. Since the larger cysts were filled with a fluid closely resembling lymph it is perhaps safe to label this

[49] Quoted by Flint.[51]

[50] Quoted by Flint.

[51] The Bloodvessels, Angiogenesis, Reticulum and Histology of the Adrenal, Johns Hopkins Hosp. Rep., 1900, ix, 153.

[52] Zur Anatomie der Nebennieren, Arch. f. path. Anat., 1887, cix, 324.

specimen as a case of lymph cysts of the adrenal. The very prominent role played by the connective tissue in this process is in agreement with the views of Ribbert,[53] who has emphasized the independent growth of connective tissue in lymphangiomatous and cystic processes. The dilatation of the spaces between the otherwise normal adrenal cells is best interpreted not as a growth of lymphatic spaces resulting eventually in cyst formation but rather as a dilatation of blood and lymph circulation produced by the large cysts.

Many of the spaces and small cysts as previously mentioned were filled with blood. In some sections these pictures were so prominent as to cast a suspicion that we are actually dealing here with a hemangiomatous process. These findings, however, were not constant enough to warrant this diagnosis, but they do indicate that the bloodvessels as well as the lymphatics have played a role in the process.

A brief summary of the pathological findings in this case show:

1. A huge hemangioma of the liver weighing nearly one-half (4.9) of the entire weight of the patient. This hemangioma is a growing tumor, an example of a true hemangioblastoma.
2. Two hemangiomata of the skull, located in the temporal bones.
3. Multiple cysts of both adrenals, apparently the result of congenital disturbances of growth in which connective-tissue lymphatics and bloodvessels have all played a role. Degenerative changes are very marked.

AN OPERABLE TUMOR INVOLVING THE GASSERIAN GANGLION.

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My experience with tumors of the Gasserian ganglion includes 3 of 43 recorded cases or 3 of the 13 cases in which the tumor was exposed on the operating table. The nomenclature "tumors of the Gasserian ganglion," I believe is misleading, since, as a matter of record, with few exceptions, all tumors so designated are tumors of the middle or posterior fossa, with only coincidental involvement of the ganglion and not infrequently of other contiguous nerves. With three exceptions the "tumors of the Gasserian ganglion," so called, exposed on the operating table, have been inoperable tumors of the middle fossa. Of the 3 cases in my clinic the tumor in 2 hitherto recorded (Case II and Case III) was inoperable; the third case was of interest

[53] Ueber Bau, Wachsthum und Genese der Angiome nebst Bemerkungen über Cystenbildung, Arch. f. path. Anat., 1898, cli, 26.

for two reasons: (1) because the operation was performed within three months of the appearance of symptoms; (2) because the growth was limited in size and well within the bounds of "operability."

The patient, a man, aged fifty-three years, was admitted to my service at the University Hospital, December 22, 1916 (File No. 33568). He had been suffering for three months from pain in the distribution of the second division of the left trigeminal nerve, which was at first "jumpy" in character, later becoming more intense. This was followed by numbness in the upper lip and was associated with or followed by neuralgia above the left eye. The case was regarded as one of trigeminal neuralgia. Two successive alcoholic injections only partially relieved the pain and the patient preferred a radical operation to repeated injections.

Operation. January 8, 1917, under ether anesthesia the ganglion was approached through a butterfly incision according to my usual technic. The middle meningeal artery was exposed and divided and the foramen spinosum blocked with cotton. Upon reflecting the dura from the surface of the ganglion an almond-shaped, encapsulated growth, overlying the ganglion and appearing to take its origin from the latter structure, was revealed. There was no difficulty in separating the dura from the ganglion throughout the greater portion of its circumference, but in the neighborhood of the second division and of the sensory root the tumor was firmly adherent. In order that we might discontinue the ether and to prevent a return of pain should the tumor recur the sensory root was avulsed. The tumor was removed *in toto* and afterward the outer two-thirds of the ganglion was taken away because of the possibility of its being infiltrated with tumor cells.

The results of the operation were eminently satisfactory to the patient; his exuberance of spirit when wholly relieved of pain was a source of amusement to all who saw him in the hospital. The wound healed *per primam* and the patient was discharged eight days after the operation.

Pathological diagnosis: endothelioma. The specimen (Fig. 2) consisted of an oval, pear-shaped mass of tissue measuring 2.5 x 1 x 1 cm. At one pole the tumor measured 0.5 cm. in diameter and gradually tapered until at its expanded extremity it measured 1.3 x 1 cm. The thin upper end was dark red in color, the globular end pale white, the whole mass being firm in consistency. Section through the tumor showed a homogeneous white surface which represented the globular expansion, and this portion seemed to be circumscribed and distinct from the narrow upper pole to which it was attached. Microscopic examination disclosed a process which consisted of a fibrous connective-tissue stroma, present in a large amount, between the meshes of which appeared numerous cells. The cells varied in shape, some being spindle, others vesicular. The entire picture presented a distinctly polymorphous character. The cells took a deep nuclear stain; the protoplasm was well stained with

eosin; the cells were arranged in small clumps in many areas, occurring in the form of whorls after the manner of tumors springing from endothelium.

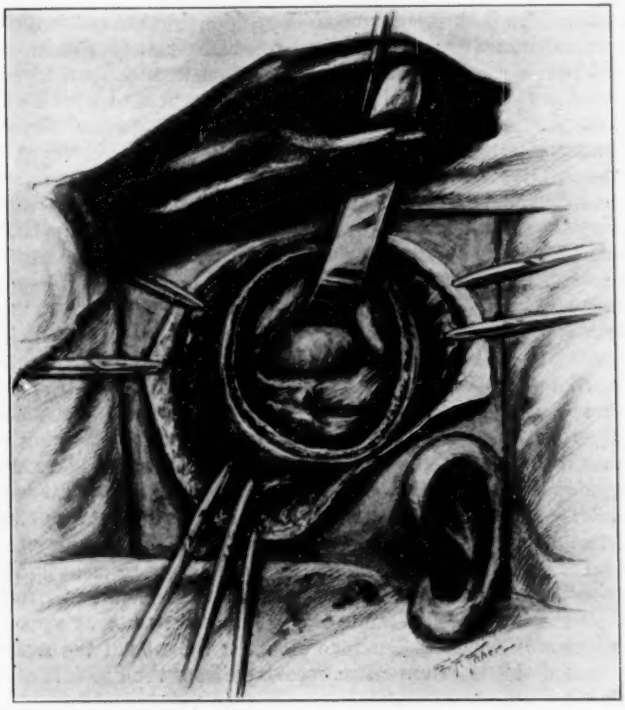


FIG. 1.—Drawing showing relation of the Gasserian ganglion to the third division and the superior surface of the ganglion, drawn in the course of the operation.

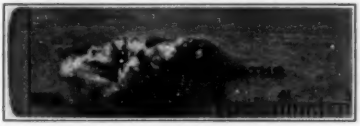


FIG. 2.—Photograph of tumor after removal.

Two of the author's cases have already been recorded by Spiller.[1] Briefly the conditions were as follows:

CASE II.—The patient, a man, aged twenty-five years, was referred to my service at the University Hospital, by Dr. William G. Spiller, April 11, 1907. In the winter previous to admission the patient suffered from paralysis of the right trigeminal nerve, accompanied by severe pain. Three months before admission the right

[1] AM. JOUR. MED. SC., 1908, cxxxvi, 721.

optic nerve was seriously involved and later the left, until complete blindness resulted. There was deafness on both sides and bilateral impairment of the sense of smell; headache became most intense; the patient vomited a number of times and the left arm became paretic. The patient was unconscious upon admission. A lumbar puncture showed the cerebrospinal pressure equal to 27 mm. Hg., and 15 c.c. of cerebrospinal fluid were removed. A temporal decompression was done on each side, but the patient died within a few hours. At the autopsy a tumor measuring 4 cm. in either direction and extending 3 cm. into the brain was found growing from the dura, covering the floor of the middle fossa as far forward as the right sphenoidal fissure, also the inner part of the petrous portion of the temporal bone in the posterior fossa, extending over the basilar process as a flat growth as far as the left posterior clinoid process. The tumor was most developed at the site of the right Gasserian ganglion, which was entirely obliterated, and the right fifth, third, fourth and sixth nerves were enveloped in it.

CASE III.—The patient, a man, aged forty-three years, was referred to my service at the University Hospital March 7, 1906. He had suffered from severe pain and weakness in the distribution of the right trigeminal nerve for about five months. Hearing was impaired on the right side and the pupils were unequal and responded sluggishly to light; there was weakness of the right external rectus muscle, some retraction of the right eyeball and narrowing of the right palpebral fissure. An enlarged lymph node removed for examination revealed an endothelioma. The pain became so intense that an attempt at relief by operation seemed imperative. At the operation, April 5, 1906, I found an inoperable growth, only a portion of which was removed, but before closing the wound the sensory root was divided. The patient recovered from the operation, and until his death, two months later, the pain was bearable. At the autopsy the tumor mass was found to extend from the base of the skull into the temporal lobe, which was edematous and soft; the mass was yellowish in color and easily separable from the brain. The tumor occupied the region of the right Gasserian ganglion and not even a remnant of ganglion tissue could be seen.

While the clinical picture of tumors of the Gasserian ganglion is not always definite, nevertheless there are certain signs and symptoms which may be regarded as characteristic. The first clinical manifestations are almost invariably subjective and objective sensory disturbances in the distribution of the trigeminal nerve on the side of the lesion. Pain is usually experienced in the distribution of the three branches almost simultaneously, although occasionally, if the tumor be small and encapsulated, the pain may be limited for some time to that part of the nerve whose fibers are affected in the ganglion, as in Case I of my series. The pain, which is severe from the first, is continuous, of constantly increasing intensity, with frequent paroxysmal exacerbations. Objective sensory disturb-

ances also appear early in the same distribution, first in the form of hyperesthesia, later of hypesthesia and hypalgesia, gradually being transformed to anesthesia and analgesia. These are accompanied by trophic disturbances of the cornea, terminating in neuroparalytic keratitis and sensory disturbances in the tongue and mucous membrane of the nose on the corresponding side. The motor branch of the trigeminal becomes paralyzed sooner or later, causing paresis or paralysis of the masseters, temporals and pterygoids.

It may happen, as in Case I, that the trigeminal is the only cranial nerve implicated, but we frequently find, particularly in cases in which the tumor has assumed large dimensions, signs of oculomotor paralysis and involvement of the fourth and sixth nerves, unilateral visual disturbances on the side of the lesion, disturbances of the sense of smell and occasionally involvement of the seventh and eighth nerves. According to Spiller,[2] tumors of this region are prone to extend in the form of a flat growth along the base of the middle fossa, thus involving the temporal lobe without infiltrating the brain, although they may be closely adherent to it. A manifestation of this extension has been noted in disturbance of the sense of smell, but this can hardly be regarded as a regional symptom; it may be due to an extension of the growth forward or merely to the pressure incident to increased intracranial tension. Nor can the signs of increased intracranial tension in general be looked upon as significant, since they are an almost constant accompaniment of brain tumor of any locality. Paresis of the extremities has been noted in several cases and hemiplegia in one. The finding of enlarged cervical lymph nodes, emphasized by some authors, merely indicates the presence of a tumor and throws no light upon its location; it may be of use, however, in the presence of other localizing signs. Percussion of the skull has been found to be of value by several. In the case of Hofmeister and Meyer[3] percussion produced severe pain in the right temporal region, and a deep tone, which was limited to a spot the size of a mark, immediately over and in front of the right auditory meatus.

STATISTICAL TABLE FROM AN ANALYSIS OF TWENTY-NINE CASES.

Age of patient.	
20 to 30 years	7
30 to 40 "	6
40 to 50 "	7
50 to 60 "	1
70 to 80 "	1
Left or right side.	
Left side	15
Right side	6
Primary, etc.	
Primary	9
Secondary	9
Doubtful	3

[2] Loc. cit. [3] Deutsch. Ztschr. f. Nervenheilk., 1906, xxx, 206.

REGIONAL SYMPTOMS.

1. N. trigeminus.	
Pain in trigeminal distribution	8
Hyperalgesia	1
Pain and anesthesia	4
Paresthesia	1
Anesthesia	3
Anesthesia confined to left cornea and left half of tongue	1
Loss of corneal reflex	4
2. N. oculomotor.	
Ptosis: Unilateral	3
Bilateral	2
3. N. abducens.	
Diplopia	3

NEIGHBORHOOD SYMPTOMS.

Deafness	1
Tinnitus	1
Hemiplegia	3
Paraplegia	3

SYMPTOMS OF INCREASED INTRACRANIAL TENSION.

Headache	4
Dizziness	2
Vomiting	1
Ataxia	2

It is not difficult to understand that occasionally tumors involving the Gasserian ganglion are confused with tumors of the cerebellopontile angle, or indeed with certain inflammatory processes involving the base of the brain. The Gasserian ganglion, situated as it is in the middle fossa on the anterior surface of the petrous portion of the temporal bone and protected by its dural envelope, is seldom invaded by tumors arising in the cerebellopontile angle. Nevertheless, the root of the trigeminal nerve, as it makes its exit from the pons, may be so involved as to cause both subjective and objective sensory disturbances, which can scarcely be differentiated from those caused by implication of the ganglion itself. Although a tumor of the Gasserian ganglion may occasionally implicate the eighth nerve, deafness seldom develops until very late in the course of the disease, and only after the severe subjective and objective disturbances of the trigeminal nerve have persisted for some time. On the other hand, eighth nerve involvement is not unusual in "recess" tumors, and in "acoustic" tumors the nerve is of course uniformly involved. Of other manifestations of cerebellopontile tumors ataxia has also been observed in tumors of the Gasserian ganglion, but only in exceptional cases.

It is sometimes difficult to distinguish at first between a tumor of the Gasserian ganglion and a syphilitic or tuberculous meningitis involving the ganglion, but by appropriate examinations the presence or absence of a syphilitic or tuberculous process may be determined. Moreover, such chronic inflammatory processes develop slowly and may even completely subside for a time, while

tumors in this region usually grow rapidly and soon assume large dimensions.

The proportion of cases of trigeminal neuralgia, so called, to tumors involving the ganglion of Gasser is, in my experience, about 100 to 1; that is to say, I have seen but 3 cases of tumor to over 300 cases of neuralgia. Symptomatically, tumors of the Gasserian ganglion are, at least in the early stages, often confused with "tic douloureux." In tumors there is often a combination of pain and anesthesia; the pain more frequently involves the entire distribution of the trigeminal nerve, is of greater intensity and usually without the intervals of freedom so characteristic of trigeminal neuralgia. In tumors the corneal reflex is often absent, the muscles of mastication affected, other cranial nerves, particularly the third and sixth, are implicated, and there are the neighborhood symptoms and the signs of increased intracranial tension.

In a careful review of the literature there seem to be all told but 43 recorded cases of tumor of the Gasserian ganglion, 30 revealed at autopsy and 13 on the operating table.

CHRONOLOGICAL TABLE OF THE THIRTEEN RECORDED OPERATIONS UPON "TUMORS OF THE GASSERIAN GANGLION."

Date.	Recorder.	Operator.	No.
1895	Krogius	Krogius	1
1900	Keen	Keen	1
1906	Hofmeister	Hofmeister	1
1906	Spiller	Frazier	2
1907	Marchand	Marchand	1
1908	Giani	Durante	1
1911	Hartig	Krause	3
1913	B. Sachs	Berg	1
1916	E. Sachs	E. Sachs	1
1918	Frazier	Frazier	1
Total			13

The great majority of these 43 recorded cases have been either sarcoma or endothelioma, as will be seen in the accompanying table:

Sarcoma	15
Endothelioma	10
Carcinoma	3
Glioma	3
Gumma	2
Fibroma	1
Neurocyst	1
Aneurysm	1
No diagnosis	7
	43

According to Hellsten[4] the ganglion possesses a peculiar resistance to the invasion of tumors. Practically all take their origin, not from the Gasserian ganglion, but from the dura or some other structure of the middle fossa and involve the ganglion only coincidently. While at first they may be limited to the region of the ganglion, they

[4] Deutsch. Ztschr. f. Nervenheilk., 1914, lii, 290.

expand often in the form of a flat growth along the floor of the middle fossa, occasionally invading the orbit, the sella turcica or even the posterior fossa.

Since the first operation by Krogius,[5] in 1895, there have been reported, including my own, 13 cases of tumor of the Gasserian ganglion which have been exposed at operation; of this number 10 were large inoperable growths and the death-rate was high. In but 3 cases was the tumor operable in the sense that it could be completely removed. These were the cases of Berg, Sachs and the author. In the case of Sachs and Berg a burning sensation had been experienced eleven months prior to operation. A large endothelioma, involving the entire ganglion and all its branches, was exposed and removed. The patient made a good recovery and two months after the operation was free from pain and complained of nothing save loss of taste on the left side.

In the writer's case the operation was performed within three months of the first symptom. The patient was seen fifteen months after the operation and, apart from certain paresthesias, which might well have been due to avulsion of the sensory root, there were no signs of recurrence.

In those 3 cases in which the tumor was strictly within operable limits there were no operative fatalities. On the other hand, when a radical operation was ambitiously but unwisely attempted the results were in most instances disastrous. When the lesion has advanced beyond the point where an attempt at removal can be made with propriety one should not shrink from operation, if only as a measure of temporary relief. To this end avulsion of the sensory root for the relief of pain or subtemporal decompression for the relief of pressure may give the patient a respite for which he may be most grateful.

SAHLI'S VOLUME SPHYGMOBOLOMETER: A RECENT IMPROVEMENT OVER THE OLDER PRESSURE SPHYGMOBOLOMETER.[1]

By Nathaniel Bowditch Potter, M.D.

until 1918, professor of clinical medicine, columbia university (college of physicians and surgeons); visiting physician to the new york city hospital; chief of medical department, st. mark's hospital; consulting physician to the french hospital, the new york throat, nose and lung hospital and the central islip state hospital; director of the memorial laboratory and clinic for the study and treatment of nephritis, gout and diabetes at santa barbara, california.

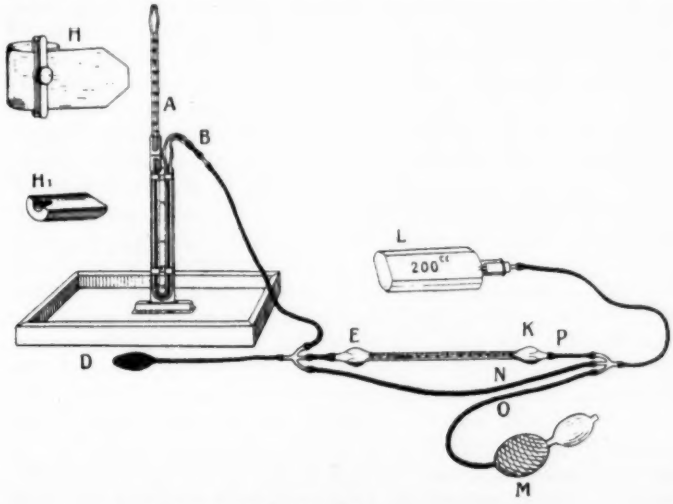
Endeavoring to improve the latest modification of his sphygmobolometer, to simplify the entire procedure and to further the clinical

[5] Revue de Chir., 1896, xvi, 434.

[1] Cf. Potter, N. B.: Jour. Am. Med. Assn., April 19, 1913, p. 1211.

applicability of this dynamic method of studying the pulse, Sahli has recently introduced[2] the volumesphygmobolometer (volume-bolometer) as distinguished from the pressuresphygmobolometer (pressurebolometer). The latter directly estimates the *pulse work* (*arbeit*), whereas the new instrument measures the *pulse volume* and only indirectly, with the aid of a simple table, the *pulse work*. After many months' experience with this latest model, including a careful comparison with the former (pressurebolometer), the writer has become entirely convinced of its superiority, both in simplicity and accuracy. Many of the defects and drawbacks of the pressure instrument[3] have been obviated or at least minimized, and the determination of the *pulse volume* and *work* has been made so simple that the distinguished clinician's plea for a more general utilization of the instrument and method in the study of pulse dynamics seems well worth echoing in America. It is outside the scope of this communication to discuss the clinical utility of the determinations revealed by this method, or to more than once more mention Sahli's apt contrast between them as *dynamic* and blood-pressure figures as *static* estimations, to attempt to estimate the horse-power of a locomotive from the measurement of the steam pressure in the boiler. In what follows the writer will merely describe the volumebolometer and its application, and in order to justify the entire method, enumerate a few values obtained with the old as contrasted with the new instrument.

The new apparatus, coupled together, is represented in the following cut:



[2] Arch. f. klin. Med., 1914, Bd. cxv.
[3] Outlined in a communication to be published shortly.

It consists of two parts: Sahli's pocket mercury manometer (1914 model, *AB*), simplified by the omission of the caliber narrowing or throttling at the bend of the U-tube, and the same cuff (*H*), hard-rubber plate (H_1), pelotte (*D*), connecting tubing with a double rubber bulb (*M*) instead of the syringe, and a modified index manometer (*EK*). The latter, an index volumeter, alone requires description. Terminating in ampullæ open at each end (*E* and *K*) the capillary tube, with a large bore, is plainly divided into much longer subdivisions than the mercury manometer. It contains about 0.2 c.c. colored petroleum, indicating not linear centimeters but hundredths of cubic centimeters. The pelotte is applied flat and empty, as with the older instrument, and without any pressure in the system. By means of two triple Y-glass connections, and the same accurately calibrated, stiff rubber tubing (1.5 mm. in diameter), one ampulla (*E*) is coupled to the mercury manometer (*A*); to the pelotte (*B*) and with flexible tubing to its fellow ampulla (*K*); the other (*K*) to a 200 c.c. empty bottle (*L*) fitted with a perforated rubber stopper and glass tube; with soft compressible rubber tubing to a double rubber bulb (*M*) and to its fellow ampulla (*E*). Inflation of the bulb increases the system's pressure but slowly because of the inclusion of the relatively large air space in the bottle, and does not affect the position of the colored index in the capillary tube because of the free communication of the two terminating ampullæ by the compressible tube (*N*). After application of the pelotte to the radial artery in the usual way and the introduction of a sufficient pressure in the system the index will begin to pulsate as soon as this latter tube is tightly compressed by the finger of the examiner, thus excluding the large air space of the reservoir and limiting the action of the pulse to that portion of the space to the left of the index. With an open tube (*N*), tipping the index manometer will readily depress the colored index by gravity and so enable the examiner to collect and form the index at or near the middle of the manometer. Just where this is does not matter, but if the index is too long some of the petroleum can be quickly returned to one of the two ampullæ by gravity flow, and if "split" into several indices, though this is of no special disadvantage, the superfluous smaller ones emptied into an ampulla in the same simple fashion. It is also very easy to destroy the index if it is desirable to form another. This is done by raising the manometer to a vertical or oblique position, pinching the tube (*N*) and gently pumping with the bulb. To release the pressure from the system the rubber stopper is withdrawn from the bottle, although the practically constant leaking of the bulb is usually sufficient. To avoid bursting or unduly distending the delicate rubber of the pelotte, no pressure should be exerted in the system until after the snug application of plate and cuff on the wrist. The same rules for testing the impermeability of the system as applied to the older method hold good for this apparatus, but are much less essential

because inflation of the bulb will quickly correct any leakage of air, and the results in volumebolometry are independent of the volume of the contained air.

DIRECT ESTIMATION OF THE VOLUME (V) OF THE "OPTIMAL DAMMED" PULSE (THE CLINICAL "PULSE VOLUME") (Grösse). After applying the pelotte to the radial artery, securing it in position there firmly, establishing the index and inflating with the bulb until enough pressure exists in the system to evoke a pulsation of the index, this pressure is read upon the mercury manometer. Each further increase of pressure is accompanied by pinching the two flexible rubber tubes at *N* and at *O* in order to judge the size of the pulsations of the index. If the latter is dislocated along the capillary tube a leak exists upon the side of the system toward which it moves and should be corrected. As the pressure in the system is gradually increased the pulsations lengthen, then remain for a time equal and finally diminish. The *optimal pressure* corresponds to the pressure in the mercury manometer just before which these pulsations begin to diminish again in size: in other words, the point at which the energy of the pulse beats is most completely transmitted through the system. The pulsations of the index are then read off the subdivisions of the capillary tube in hundredths of cubic centimeters. As stated above the relative position of the pulsating index in the capillary tube is of no import.

Just as with *pressurebolometry* one can advantageously control the measurement by now repeating it backward, so to speak, *i. e.*, by overstepping the point of maximum pulsation, allowing the pressure in the system to slowly decrease by means of the gradual leaking of the bulb and connections until a point is noted at which the excursions suddenly begin to once more increase. This is again the *optimal pressure*.

These excursions at optimal pressure are an absolute measure (hundredths cubic centimeters) *of the volume of the optimally dammed pulse;* in other words, what we have always been accustomed to roughly estimate with the palpating finger and speak of as the size (grösse) of the pulse. This is of course merely a relative measurement of the size of the circulation based upon the pulse in that portion of the radial artery included under the inflated pelotte.[4] In estimating the size of the circulation, *pulse frequency* must of course be considered as well.

The detail to be remembered before reading the index is always to exclude the bulb from the system by pinching the tube at *O* as well as at *N*, otherwise the excursions would not exactly equal the volume of the dammed pulse.

Now these excursions which measure the dammed pulse are quite large and very striking, may even attain several centimeters in length,

[4] Cf. Sahli: Deutsch. Arch. f. klin. Med., 1914, 3d cxv.

and hence may be exceedingly rapid, so that sometimes an irregular movement or shaking results and produces the impression of too large a pulse volume. This is readily detected by noting that the meniscus of the index does not pause for an instant at the point at which the index is read but exhibits vibrating individual movements. To prevent this the index is shortened to 1 cm. or less by allowing part of it to flow into one of the ampullæ.

Estimation of the Pulse Work (Arbeit). The *work* (*A*) is reckoned according to the following formula:

A = V × P × 13.6 gram centimeters in which:
A = work,
V = volume of the dammed pulse expressed in cubic centimeters.
P = optimal pressure expressed in cubic centimeters Hg.
13.6 = specific gravity of mercury.

The accompanying table will facilitate this computation:

P. (cm. Hg.)	P. × 13.6.	P. (cm. Hg.)	P. × 13.6.	P. (cm. Hg.)	P. × 13.6.
1	13.6	11	149.6	21	285.6
2	27.2	12	163.2	22	299.2
3	40.8	13	176.8	23	312.8
4	54.4	14	190.4	24	326.4
5	68.0	15	204.0	25	240.0
6	81.6	16	217.6	26	353.6
7	95.2	17	231.2	27	367.2
8	108.8	18	244.8	28	380.8
9	122.4	19	258.4	29	394.4
10	136.0	20	272.0	30	408.0

The Superiority of Volumebolometry to Pressurebolometry. As contrasted with the pressurebolometric equations the barometric pressure is entirely disregarded in volumebolometry, an advantage when employing this clinical method at elevations above 3000 feet. Another advantage is that the values are much less dependent upon an optimal application of the cuff, since in virtue of the large air space the increase of pressure in the system to produce the pulsations is a minimal one. It is advisable, however, even with this method, to secure an optimal cuff application, but this is accomplished by comparatively moderate tension of the cuff.

THE DIAGNOSIS OF CHRONIC APPENDICITIS.[1]

By William Fitch Cheney, M.D.,
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The recognition of chronic appendicitis presents many difficulties: on the one hand because its own manifestations are so variable,

[1] Read before the Nevada State Medical Society, at Reno, Nevada.

and on the other hand because so many conditions simulate it. Every patient seeking advice for stomach trouble or indigestion or abdominal pain may have chronic appendicitis as a cause while many that complain of ailments more remote, such as recurring headaches, failure to gain in weight, persistent vague symptoms, such as lack of energy and incapacity for exertion, may really owe their ill health to chronic appendicitis, as shown by their return to normal after a diseased appendix has been removed. But disease of the gall-bladder, of the ovary or the Fallopian tube or of the kidney may each produce symptoms so much like those of chronic appendicitis that to escape error in diagnosis requires the utmost care. From all sides, therefore, we are beset by difficulties, and the greater the experience the greater the caution about reaching a conclusion. Although this subject has been discussed so extensively during the past decade that not much new remains to be said, nevertheless a consideration of problems as actually presented in every-day work may be of value, because they will serve to show by what methods we decide that a diseased appendix produces the symptoms for which the patient seeks advice.

How frequently is chronic appendicitis a factor in ill-health? Probably not so often as many are ready to believe. Among 2116 medical cases seen in private practice during the five years from January 1, 1912, to January 1, 1917, only 71 after careful study presented evidence sufficiently definite so that a diagnosis of chronic appendicitis could conscientiously be made. During this same period 297 cases of chronic gastric disease were seen and 62 of chronic gall-bladder disease. The conclusion has thus gradually been reached that chronic appendicitis is too often suspected as an adequate explanation for obscure digestive ailments—much more often than is justified by the fact. There is too great a tendency to convict the appendix without sufficient evidence and to advise its removal on the basis that it is a useless organ anyway, and taking it out can do no harm. Unfortunately it is also true that in many cases taking it out can do no good.

I. HISTORY. As a means of diagnosis a careful history is always of the highest value, and it is worth while to note of what these chronic appendicitis cases complain. Of the 71 observed, 31 sought advice for "stomach trouble," 25 for pain in the abdomen, 4 for persistent abdominal soreness and tenderness, 1 for "gas in the bowels," but 7 complained chiefly of recurring headaches and 3 of lack of energy and vitality.

Stomach Trouble. Unfortunately the stomach symptoms are not always the same, so that no conclusion can be reached from this part of the story alone. Some of the cases resemble gastric ulcer in their chronicity and periodicity; with gastric attacks lasting for weeks or months, followed by days, weeks or months of remission or complete intermission of symptoms; and in the character of their

symptoms, with burning pain in the epigastrium or right or left hypochondrium as the chief complaint, this pain coming on one to four hours after eating, accompanied by belching, waterbrash and nausea. This group is found, as will be shown later, to have a reflex hyperchlorhydria as the cause of their gastric suffering. A smaller group of cases resembles chronic gastritis, with distress soon after taking food, a sense of fulness and distention but not of pain, much belching of gas and frequently regurgitation of a mouthful of food, this process going on over and over after each meal. This group shows on analysis a subacidity, but in some there must be the added factor of pylorospasm, reflex from the diseased appendix.

The history of these cases taken by itself may create suspicion of the appendix, but that is all; other symptoms and other evidence must be sought for in various ways to be described before reasonable certainty can be reached. The difficulty is that the patient's complaint about the stomach is frequently so loud and persistent that it leads the physician himself astray, directing all his attention to this organ instead of to the one really diseased.

Pain in the Abdomen. Twenty-five patients who came for advice about this symptom were found to belong in the group of chronic appendicitis. In some the pain was definitely referred to the right lower quadrant, present constantly or in spells; in others it was not so well defined but referred simply to the abdomen or to the bowels. Sometimes complaint was made also of tenderness and soreness, increased by jarring or jolting, as by riding on horseback or in an automobile. This pain was variously described as an ache, a hurting, a sense of distention or simply as soreness. It might be very annoying for days and then for days might practically disappear. In every instance this had gone on so for months or for years. Such a story, while in no way diagnostic, is extremely suggestive, and no one hearing it would probably fail to think of chronic appendicitis as a likely cause. The same is true of the four other histories in which abdominal soreness and tenderness were the chief complaints. Different patients express their discomfort in different ways, but with all these variations of the story of persistent abdominal pain and soreness the appendix as a cause should be given almost the first thought.

Symptoms Outside the Abdomen. When the patient's story is of trouble in the abdomen it is not likely the appendix would be forgotten in the search for an explanation. But 7 in the group here reviewed sought advice especially for recurring headaches and 3 for lack of energy and vitality. With such complaints, chronic appendicitis would scarcely be suspected; and yet these and other symptoms in remote parts of the body may result as the chief manifestation. The explanation perhaps lies in the associated constipation due to adhesions, with resultant auto-intoxication; b-

whatever the relation may be the fact remains that in certain of these cases to be reported, removal of a diseased appendix has relieved these remote symptoms after other methods of treatment had failed.

Constipation. As regards this symptom it is too common an ailment to have any significance in relation to chronic appendicitis. The two conditions are often associated, but the question then is which preceded, which is cause and which effect. It is also being discovered gradually, as roentgen-ray plates are being made more frequently, that both the constipation and the chronic appendicitis may be secondary to prolapse of the cecum and colon and consequent stasis of contents. Chronic constipation may be due to mechanical difficulties produced by adhesions about a chronically inflamed appendix, but may be due, and probably more often is, to other factors entirely, which have likewise caused the appendix to become diseased.

Previous Acute Attacks. In any history of chronic digestive ailment a question of great importance is whether there have ever been attacks of pain in the abdomen that might have been due to acute inflammation of the appendix. These attacks may have occurred long before the patient comes for advice and may be forgotten unless sought for or they may occur from time to time simply as subacute exacerbations of the chronic disturbance or there may have been one or two previous attacks not recognized as appendicitis but called "ptomain poisoning," inflammation of the bowels, or simply "colic," and never given a thought in connection with the subsequent chronic disturbance of digestion. Such a history of previous acute attacks could be elicited in 37 of the 71 cases in this group, but not in the other 34. The significant fact lies in the absence of any such history, for it suggests that chronic appendicitis may be chronic from the beginning and that an acute onset of any sort is not essential to establish the diagnosis.

In general there is no type of history from which alone a diagnosis can be reached. Sometimes one complaint and sometimes another predominates, and sometimes there is a mixture of all those described. But other and more definite evidence must be obtained before suspicion becomes conviction.

II. Physical Signs. The evidence found on abdominal palpation to prove that chronic appendicitis exists may be very definite or very indefinite, very extensive or very slight. A palpable mass in the appendix area, varying in size or shape, like a thumb or a hen's egg or a sausage, with more or less tenderness on pressure—these are the expected findings. But experience teaches that these signs are very variable. No mass at all may be palpable, but the patient complains of intense pain when pressure is made over the usual appendix site; rigidity and muscle spasm may be present in the right lower quadrant of so great degree as to make localization

of any mass beneath impossible; or no mass or tenderness whatever may be found at one time of examination, though both may be present at another time. As is also well known the greatest tenderness may be found high up along the ascending colon, prompting one to suspect the gall-bladder; or low down in the inguinal region, leading in female patients to the conclusion that the disease is pelvic. Among the 71 patients whose histories have been reviewed, 62 presented definite physical signs in the appendix area, but 9 presented no evidence that could be interpreted to mean chronic inflammation there. Of these 9 patients, 6 proved at operation and 1 at autopsy to have chronic appendicitis. The other 2 have never yet had operation so far as can be traced. The diagnosis was made in these cases, and operation was advised on other data to be described as we proceed; but the point to be emphasized at this time is that absence of the signs usually expected on palpation of the right lower quadrant does not prove the absence of chronic appendix inflammation.

There are several explanations to account for this failure to find what ought to be found: (1) When the appendix lies behind the cecum, firmly attached to it by adhesions, one has to palpate not only through the abdominal wall but through the cecum in order to feel what lies beneath, and this is usually impossible; (2) one of the most troublesome forms of chronic appendicitis, so far as reflex symptoms are concerned, is the atrophic or obliterative type, where repeated disease has caused the appendix to shrivel and become buried in adhesions so that no mass exists to palpate; (3) the appendix inflammation when examination is made may be so quiescent that it gives no local evidence, even though reflex symptoms in the stomach or elsewhere persist and are very annoying; but sooner or later an exacerbation occurs and then the local signs become perfectly definite.

The lesson taught by these records is clearly that no one factor in the diagnosis is conclusive. Physical examination gives accurate information more frequently than does history alone, and the two together make us more certain than either one can by itself. But it is necessary to get together all the evidence by every possible method of investigation before we can reach anything like absolute certainty.

III. Gastric Analysis. In the cases with gastric symptoms predominant one must investigate the stomach secretions, as a routine part of the examination, in order to reach a diagnosis. This was done in 39 of these patients, and in 28 hyperchlorhydria was found. In 1 the total acidity was 96, in 4 between 80 and 90, in 5 between 70 and 80, in 13 between 60 and 70, in 5 between 50 and 60. In 8 the secretion was practically normal, with total acidity 40 to 50, and in 3 it was subnormal, or below 40, with 1 case under 10. It is evident there is no diagnostic analysis to indicate chronic appen-

dicitis, though the most common finding is a hyperchlorhydria. But if this finding happens to coincide with negative and dubious physical signs about the appendix, it is more likely to be attributed to some other cause, as ulcer, and so may be a hindrance rather than an aid to diagnosis.

IV. Radiographic Examination. The value of this method in recognizing chronic appendicitis has not been generally accepted and is still in question, and the experts themselves differ as to just what findings shall be interpreted to mean a diseased appendix. Nevertheless, it seems certain that as every case suspected should be given the benefit of every possible method of investigation, roentgen-ray examination can no longer be omitted. During the past year this conviction has been adopted and acted upon, and with increasing experience in the study of plates of the cecum and appendix no one can doubt the value of them or would be satisfied to give an opinion without their assistance in reaching it.

To begin with, the radiographic examination is at least eliminative of gastric conditions that confuse the diagnosis. History and gastric analysis may point direct to ulcer of the pylorus or duodenum; but if the antrum, pylorus and cap are normal on the plates the diagnosis of ulcer is evidently dubious. No patient should ever be advised to undergo operation for ulcer unless roentgen-ray plates have first been made. The only exceptions to this rule are the emergency cases, in which recent hemorrhage or continued vomiting preclude the administration of barium mixtures or when it is imperative there should be no delay. Some of the chronic appendix cases in this group of 71 were victims of a mistaken diagnosis, because in the earlier years recorded no roentgen-ray plates had been made, and only at operation advised for ulcer was it discovered that no ulcer existed but a chronic inflammation of the appendix.

But direct evidence as well as indirect can be obtained from the plates. What one may expect to find is epitomized thus by Case:[2] (1) poor drainage; (2) localized tenderness on acute palpation done under fluorescent guidance; (3) kinking; (4) irregularities in the lumen; (5) unduly long or large appendix. Most observers agree that long delay in emptying, with retention of opaque material in the appendix after it has disappeared from the cecum, means poor drainage due to inflamed walls, and can be depended upon as a sign of great significance.

It is admitted that a diseased appendix may fail to show on the plate because it is postcecal and obscured by the opaque material in the cecum; or because it is obliterated and cannot fill; so that negative evidence does not become a bar to the diagnosis in the face of a definite history and physical signs. But localized tenderness under the fluoroscopic screen, kinking, irregularities in lumen,

[2] Interstate Med. Jour., April, 1917, p. 339.

such as clubbing, long delay in emptying, with evidence of adhesions to the bowel, all constitute positive proof of abnormality that add much to the clinical picture. The only danger is that this method of examination will be accepted by the lazy man as a short cut to diagnosis, to the exclusion of other and older methods, such as a detailed history, careful palpation of the abdomen and gastric analyses. The value of radiographic examination is great in the diagnosis of chronic appendicitis, and no investigation at the present day is complete without it; but it is only a part and can never become the whole.

V. Operation. This method is not advised for diagnosis, but after diagnosis has been made it has been found a valuable method for revision. Out of the 71 cases in this group, operation was done on only 32 under direct observation here or as reported by the operator to whom they were referred. Others undoubtedly came to operation, but no record is at hand of what was found. The most valuable lessons have been learned from these operated cases, not so much by confirmation of conditions as predicted, but more by the additional information thus acquired, at times different entirely from what had been expected. A review of some of these cases will best serve to call attention to routine methods of diagnosis, to some of the common errors and to the problems presented in differential diagnosis.

1. *Obvious Cases.* A certain number of these patients present an easily recognized typical picture that can scarcely be mistaken, and of such the following is an instance.

Case History. A man, aged thirty years, first seen in October, 1912, sought advice for "stomach trouble." He had been annoyed at intervals for two years, his attacks coming once a month or once in two months and lasting about a week. At these times he complained of burning pain in his right side, at the edge of the ribs, appearing two to four hours after meals, with belching, nausea and heartburn. In addition to this story about his stomach he had another, of an attack in August, 1910, characterized by cramps in the abdomen and diarrhea, lasting for two days, and two months later of a similar attack, with much abdominal pain. Four months after that he began to have more constant pain in the right side of his abdomen, with tenderness to touch; and ever since he had had this pain more or less persistently. Any jarring or jolting, as in riding horseback, would start the pain. Once he had such a severe attack of this pain that he had to quit work and go to bed. This patient's stomach showed a hyperchlorhydria, with total acidity 60, free HCl 28, combined HCl 24; and he had in his appendix area a mass the size of a hen's egg, very tender on manipulation. Operation at the time was declined and for a year he tried to get along with diet, laxatives, olive oil and alkalies. But he did not improve, and finally was operated on in December, 1913, when an extensively

inflamed appendix was removed. After that his symptoms all disappeared.

If all cases presented symptoms and signs like the foregoing one would seldom have any difficulty in recognizing their meaning, but many variations from this type occur. Perhaps the greatest difficulty of all arises when stomach complaints predominate and any history or physical signs pointing to appendix disease are for a long time lacking. The following case histories bring this out.

2. *Unexplained Gastric Cases.* A man, aged twenty-eight years, seen in January, 1915, complained only of stomach trouble, which had existed for four years intermittently. There were intervals when his stomach seemed perfectly normal. His spells varied in duration, averaging several weeks, but had gradually become more frequent. At these times he had good appetite, but soon after eating gas formed, his stomach seemed to swell, he belched much gas and had a dull pain over his stomach. Eating the next meal relieved for about an hour, then the trouble began again. His bowels were obstinately constipated, but no history could be elicited of any attacks that could be interpreted as acute appendicitis nor of any pain in the appendix area. The stomach showed hyperchlorhydria, in explanation of his symptoms, but there were absolutely no signs in the right lower quadrant that could be taken to mean a diseased appendix. A few months later, however, in April, 1915, he had a sudden attack of acute purulent appendicitis, necessitating immediate operation, when it was found than an old chronic inflammation had long preceded the acute attack.

A large fat man seen in February, 1914, said his stomach had troubled him constantly for the past five or six years. He had no appetite at all; as soon as he ate he felt like vomiting; at least once every day he did vomit what he had eaten at the previous meal; he often felt nauseated on first rising, before taking any food; and when he did not get rid of a meal, felt he would be better if it was out, because it caused so much heaviness and distress, with belching of gas. This patient was obstinately constipated and never had a movement without physic. Recently he had noted some feeling of fulness in the right side of his abdomen if his bowels did not move, but never had any severe pain there. Palpation showed tenderness on deep pressure over the appendix, but no mass of any kind could be felt. The stomach contents contained an abundance of thick ropy mucus and showed a hyperchlorhydria, with total acidity 70, free HCl 50 and combined HCl 10. The only definite findings were gastric, with nothing to justify a diagnosis of chronic appendicitis, even though it was suspected. This patient's symptoms persisted in spite of treatment, until finally he had an acute attack of appendicitis in July, 1914, necessitating immediate operation, which showed an appendix kinked and bound down by many old adhesions. After its removal the gastric symptoms all disappeared.

A girl, aged sixteen years, seen in October, 1915, sought advice for stomach trouble of long duration, with severe headaches, dizziness and lack of energy. A year before she had her tonsils removed and a bony growth from her nose, because she was told the operation would restore her health, but it did no good. She continued to complain that everything she ate disagreed and gave her pain in her left side under the ribs. These pains came on about a half-hour after eating, especially after eating sour food, such as tomatoes or fruits. She had headaches almost all the time, with dizziness, and her bowels were always constipated. Her stomach showed a hyperchlorhydria, with total acidity 64, free HCl 20 and combined HCl 32. At this time she had no complaint to make of her abdomen, and examination gave no evidence of appendix inflammation. But she continued to be troubled by sour stomach in spite of diet and laxatives, and the following December complained for the first time of pains lower down in the bowels on the right side. Finally, early in January, she had an acute attack of appendicitis, necessitating immediate operation, and this showed old chronic adhesions, indicating that the recent attack was not the first.

In all three of these cases whose histories have been related, roentgen-ray plates of stomach and intestines would have thrown light on the real pathology present, and would have aided in reaching a correct diagnosis before the final acute attack. In all such unexplained gastric cases there is a cause, and even though no appendix evidence is found at one examination it may appear at another, while roentgen-ray plates may show trouble with the appendix even when physical examination is dubious.

3. *Cases Simulating Ulcer.* In still another group of cases the clinical history and the stomach analysis appear to speak so positively for gastric or duodenal ulcer, while the physical examination of the appendix region is persistently negative, that the case seems too clear for doubt. Here again error can now be avoided by roentgen-ray plates, but this was not appreciated in the earlier years that this report covers. Instances of such wrongly diagnosed cases are the following:

A physician, aged thirty-six years, who consulted me in February, 1914, had suffered ever since he was eighteen years from severe attacks called "gastralgia," characterized by heartburn, waterbrash, sour stomach and gas. He was always thin, slender and neurasthenic. His stomach would have periods of improvement, then again would relapse, and during all these years he had never been entirely free of his indigestion. At the time he sought advice he had suffered, especially for six weeks, with pain coming on several hours after food, particularly at night, so severe he could not sleep; also heartburn, sour regurgitations, belching of gas and nausea. Physical examination showed rigidity and tenseness of the abdominal wall over the upper half, more in the right hypochondrium than

elsewhere; great tenderness there on pressure, which increased his pain; but no tenderness or rigidity elsewhere. Stomach analyses made repeatedly throughout twelve years previous to his consulting me, as well as at this time, showed always a high-grade hyperchlorhydria. Operation advised for duodenal ulcer proved conclusively there was no ulcer in either the duodenum or the stomach, but a chronic appendicitis was found, of obliterative type, with the remains of the appendix very small, hard and fibrous and buried in a mass of adhesions. After its removal he had no further dyspepsia. Within a year he gained forty pounds in weight and correspondingly in energy and efficiency.

A man, aged forty years, also seen in February, 1914, complained of stomach trouble for years past: soreness over the stomach, recurring "bilious spells," with ravenous hunger, pain over one eye, sick stomach and vomiting, and at all times weakness of digestion. He had had also repeated spells during the previous five years, characterized by severe pain in the pit of the stomach coming on before meals and relieved by eating; such spells lasted several months at a time, with intervals for months when there was no pain at all. He always had a ravenous appetite, ate very heartily, but was hungry again in three or four hours, no matter how much he ate. This man was another tall, slender, lanky individual, with a loud succussion splash and considerable tenderness over his stomach, but positively no palpable mass or tenderness over his appendix area. His stomach contents showed an excessive hyperchlorhydria, the total acidity 90, the free HCl 40 and the combined HCl 20. Operation was advised for ulcer and was performed, but no ulcer of stomach or duodenum was found. The appendix was then investigated and found to be bound down and kinked, with many old adhesions about it—a typical chronic inflammation of long standing.

Both of the foregoing cases would now be recognized before operation by negative radiographic plates of the stomach and the duodenum and by more or less positive findings about the cecum and appendix. As stated previously, and now emphasized again, no operation for ulcer is in these days justifiable unless roentgen-ray plates have first been made and studied.

4. *Cases Simulating Gall-bladder Disease.* These cases offer one of the most difficult problems in diagnosis, and not unfrequently the correct solution is found only at the operating table. Many such errors have been made in the past and they will continue to be made in the future, though probably less frequently as fluoroscopic and radiographic examinations are employed more often. Both conditions give rise to recurring attacks of abdominal pain, with intervals of good health between. Ordinarily we depend upon the site of pain and tenderness and the direction of radiation of pain to distinguish one from the other. But an inflamed appendix pointing upward along the ascending colon may cause the greatest pain and

tenderness just below the costal margin, while the pain of biliary colic may be referred downward into the right lower quadrant instead of backward under the shoulder-blade. Either attack may make its onset with chill, followed by fever and leukocytosis; either may be accompanied by vomiting; either may be followed by transient jaundice; and either condition may give rise to reflex gastric symptoms between the acute attacks. Three cases in this group of 71 were wrongly diagnosed as gall-bladder disease, and only at operation was it discovered that the real disease was chronic appendicitis. But none of these had been given the benefit of roentgen-ray examination or the error might have been avoided.

5. *Pelvic Disease Simulating Chronic Appendicitis.* In female patients the question frequently arises whether the symptom-complex is due to disease in the appendix or in the right broad ligament, for a diseased appendix pointing downward toward the pelvic brim may cause constant pain and tenderness low down, just above Poupart's ligament, while an inflamed ovary or tube may refer its pain upward into the right lower quadrant. The following case history illustrates the difficulty in these cases about reaching a correct decision:

A woman, aged twenty-four years, seen in March, 1912, complained of attacks of stomach trouble at intervals for ten years past, the last one persisting for a year. During these she had much gas and belching after food and an unnatural, craving appetite, not long satisfied; also much nausea on waking in the morning and often during the day, coming on several hours after eating, though she never vomited. All these stomach symptoms were worse during her menstrual period. She had no pain in the stomach but had experienced several attacks of pain lower down in the abdomen. Her bowels were habitually constipated. Examination revealed slight thickening in the appendix area, but no tenderness or definite mass. Pelvic examination was negative. Stomach analysis showed a hyperchlorhydria, with total acidity 70, free HCl 20, combined HCl 30. The patient's gastric symptoms were all easily explained by her hyperchlorhydria, but the absence of gastric pain from the history and of tenderness over the stomach practically excluded ulcer, while the recurring attacks of pain in the lower abdomen, the chronic constipation and the at least suspicious findings in the appendix area were interpreted to mean chronic appendicitis, to which the hyperchlorhydria was secondary. Operation, however, revealed only slight congestion of the appendix and no evidence of previous inflammation sufficient to explain the symptoms, while an ovarian cyst was found on the right side, the size of a walnut. No other pathology was discovered. Both the appendix and the cyst were removed and the stomach trouble subsequently disappeared altogether.

Naturally the most important evidence of pelvic disease is found

by vaginal examination. But this is not always conclusive. In the first place, when the anatomical changes are slight, they may be missed unless the examination is made under an anesthetic and muscle spasm thus eliminated. In another instance the appendix itself, inflamed and tender, may hang down over the brim of the pelvis, be felt on vaginal examination and wrongly interpreted as a diseased Fallopian tube. Thirdly, it is not at all uncommon to find at operation both the appendix and the Fallopian tube diseased when only one has been recognized by previous examination. Thus errors not uncommonly occur. Either condition gives rise to long-standing pain and soreness in the right lower quadrant, with recurring acute attacks when these symptoms are greatly increased in intensity, and either may cause reflexly persistent disturbance of digestion, with hyperchlorhydria.

6. *Kidney Stone Simulating Chronic Appendicitis.* This condition is mentioned as a possibility in differential diagnosis, but it has never led to error in the cases under review. The particular source of trouble is the stone escaped from the right kidney and lodged in the ureter, causing pain and tenderness and recurring attacks of colic in the right side of the abdomen in the appendix area. But aside from the evidence afforded by a careful history, bringing out the fact of radiation of pain to the bladder or to the genitalia at some time during its exacerbations, with symptoms of urinary disturbance; aside also from negative findings on palpation over the appendix; there is the positive evidence afforded by urine analysis, disclosing pus and blood corpuscles in the sediment; and the final and unmistakable proof afforded by cystoscopy, ureteral catheterization, pyelography and roentgen-ray plates.

7. *Recurring Headaches Due to Chronic Appendicitis.* Seven patients presented themselves for recurring headaches who were found to have a diseased appendix as the only adequate explanation. These cases could be best set down as "gastric headaches," but their stomach disturbance was obviously reflex from some disease outside the stomach itself. The complaint of "sick headaches" is a common one. Frequently these headaches are found to be associated with some fault in the stomach's functions and disappear after this fault is corrected. But in a small proportion the condition underlying both the headaches and the gastric disturbance can be found in chronic appendicitis. The following is an instance of the part the appendix may play.

A man, aged forty years, sought advice in December, 1916, for headaches recurring at intervals for a number of years past, and persisting in spite of glasses worn for three years continuously, fitted to overcome eye-strain. The pain in his head gradually had grown more and more constant, at times becoming so severe he could scarcely bear it. This pain was felt sometimes through the temples, sometimes through the back of his head, sometimes all

over the top. He complained also of chronic constipation, but had a good appetite and no digestive distress. He also complained, but only when asked directly about it, of a pain in the right side of his abdomen; usually only a sense of heaviness, as if there was a big lump there; but at times this became severe pain. This man was very large and heavy. He had no evidence of nephritis, a blood-pressure within normal limits and a negative Wassermann reaction. His stomach contents showed only a slight subacidity after a test meal. In the right lower quadrant was found a very definite tender mass in the appendix area, the size of a hen's egg, constantly present at several different examinations on different days. Radiographic plates showed filling defects in the cecum and ascending colon and no barium could be caused to enter the appendix. At operation, in July, 1917, the appendix was found kinked at its base, hypertrophied and elongated, with numerous old adhesions binding it down. After its removal the pain in the head, previously constant, entirely disappeared, though medical treatment of all kinds had failed to relieve it. No attempt is made to explain how the inflamed appendix caused the headaches, but the fact remains that one disappeared with the other.

8. *Neurasthenia Due to Chronic Appendicitis.* Finally in 3 of the cases included in the group here reviewed the sole complaint was of lack of energy and vitality, and the patient's story corresponded to the condition commonly called "neurasthenia." The diagnosis of an inflamed appendix was arrived at only after routine investigation in an effort to discover why the symptoms had arisen. One of these histories will suffice to demonstrate that such a relationship may exist.

A patient, aged thirty-seven years, seen in September, 1916, complained of congestion in his head, inability to apply himself to his work, insomnia, great restlessness and general "nervous breakdown." He was a large, well-nourished man, apparently in good health, but had been compelled to give up his work as a clergyman because of his symptoms. No abnormality was found in any organ on physical examination and the stomach contents showed a normal analysis after a test-meal. No cause could be found for his symptoms except a chronic constipation. A series of roentgen-ray plates, however, made of the gastro-intestinal tract showed that the appendix filled readily with bismuth but did not empty again, retaining the bismuth even after seventy-two hours. In spite of this finding, as no evidence of chronic appendicitis could be discovered on physical examination repeatedly made, the radiographic evidence was for the time disregarded. But finally, as no improvement resulted from any treatment given and as the patient remained incapacitated for his work, removal of the appendix was advised. This was done in May, 1917. The appendix and the head of the colon were found bound down by very old and very dense adhesions. The

appendix was sharply angulated at its base, close to the bowel, and its distal portion distended and thickened. After removal of the appendix this patient made a prompt convalescence. He rapidly recovered his usual energy and desire for work, went back to it in July and is now apparently as active and vigorous as ever before in his life. Nevertheless, this case does not prove that neurasthenia is always or often due to chronic appendicitis but only that it may be in exceptional instances.

The object of all diagnosis is rational treatment, and once chronic appendicitis is diagnosed there is no cure but surgery. We wish therefore to be very certain before we advise; certain that this condition exists; certain that it is responsible for the ill health of which the patient complains; and reasonably certain that removal of the diseased appendix will restore good health. These considerations have prompted this review of the methods by which we reach a decision and of the other possibilities that must be remembered before we select the appendix as the proper point of attack.

MULTIPLE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE) AND ITS INHERITANCE: WITH DESCRIPTION OF A CASE.

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1. Classical Symptoms of Multiple Neurofibromatosis. Among the rarest of abnormal conditions of the surface of the body is that characterized by a large number of sessile or pedunculated swellings or tumors, sometimes soft and elastic, sometimes firm and tough, that vary in size from that of a millet-seed to that of a child's head. The skin over the tumors is frequently discolored, brownish or bluish, or reddish through enlarged capillaries. They may be present from birth and they may tend to grow, usually very slowly, but they rarely, if ever, regress in size. When numerous and large in one area they may become confluent. Examination shows that they are fibrous tumors, frequently containing one or more nerve fibers; or, when more deep-seated, being enlargements of the perineurium of the nerve trunks. They are due to localized cell proliferation of the connective-tissue sheaths of the nerves.

Metabolic changes frequently influence the course of the disease. The changes or pregnancy are stimulative. Thus in Meek's(1905) case "the first nodule appeared on the right shoulder during her (the propositus's) first pregnancy and steadily increased in size. During each succeeding pregnancy (but never in the interim) new growths appeared." In Hirst's(1911) case the patient (who was at the time of examination aged thirty-eight years and had numerous tumors) married at twenty-five years and became pregnant at twenty-six years. Up to this time she had only four or five tumors which had first appeared at eighteen years; during the first pregnancy they increased greatly in number.

The changes of puberty are apt to be associated with the first marked development of the tumors. In Arnozan and Prioleu's (1883) case the patient's sister noticed her tumors increasing in size after puberty, just as one of the patient's had. In Rapok's (1890) patient, a girl, aged seventeen years, the tumor of the eyelid had grown rapidly during the preceding one and a half years; note also Hirst's(1911) case. Likewise in Laignel-Lavastiné et Leroy's (1905) case the generalized tumor formation was first noticed in the female patient at eighteen years. In Czerny's(1874) history the patient's mother had a tumor in the region of the upper thoracic vertebræ, and this began to grow rapidly at twenty-six years, after her menses had, precociously, ceased.

The exciting role of various infections is somewhat supported by many reported cases. Marie(1903) laid great stress on this point. In one of the cases reported by Fraenkel and Hunt(1903) the tumors developed after typhoid fever. Rolleston(1899) reported a case in which, after an attack of pneumonia, the tumors became more numerous. Rolleston and MacNaughton(1912) reported the occurrence of the disease after the injection of diphtheria antitoxin in two sisters whose father was also a victim of the disease. Intoxication may also be an etiological factor. Tumor growth has been observed after arsenical intoxication. Our case had an attack of lead poisoning before the disease developed. An attempt has been made to connect von Recklinghausen's disease with tuberculosis. Cases in which the two conditions were associated have been recorded by Poncet(1909), Mosse(1907–8), Pic and Rebattu(1908), Pic and Gautier(1908) and Oulmont and Haller(1909). One of von Recklinghausen's patients died from hemoptysis after admission to the hospital, and at the autopsy cavities were found in the lungs together with tuberculosis of the kidneys and intestines. The case to be reported here had an old pulmonary tuberculosis. Caution has to be exercised in drawing conclusions from this association, however, since tuberculosis is so common a disease.

Frequently associated with the tendency to form tumors is another—namely, the production of pigmented spots or patches

in the skin. These, likewise, may be present from birth, but more commonly they are first noticed later. The largest may be several decimeters in diameter. The usual color is *café au lait*. The pigment spots are not unrelated causally to the tumors. Nevi or pigmented spots frequently arise first as colored moles or small tumors, which flatten out to form *café au lait* patches. The same tendencies that cause proliferation of the cells of the derma also cause a special proliferation of the pigment cells of that tissue.

Incidental to the tendency to form tumors we find a variety of other conditions which are occasionally present. These will be considered in Section 3.

Painful symptoms due to the disease are either entirely absent or they correspond more or less to those of neuralgia or neuritis. The neurofibromata may remain latent and may be first accidentally discovered during an examination, or, as in one of the cases reported by Fraenkel and Hunt(1903), revealed only at autopsy. In some cases these tumors manifest themselves by intense pain, which arises at the site of the tumors and radiates in the direction of the nerves. There is also a great tenderness on pressure. As a rule there is paresthesia, sometimes hypesthesia, in the area of distribution of the affected nerve, but rarely paralysis or atrophy. Reflex local muscular contractions may also develop, and even general convulsions of the type of reflex epilepsy. The disease had been observed in connection with epilepsy, hysterical hypochondriasis and neurasthenia, and is occasionally accompanied by sensory disturbances and mental disorders. Gastric disturbances have been noted in cases of von Recklinghausen's disease, and it is of interest that in one of these cases miliary fibromata were found postmortem in the wall of the stomach and duodenum.

The number of these nodules varies with age and constitution of the individual. They tend to increase in number, as well as in size, with age. At one extreme there may be only a solitary growth upon one nerve, at the other the number is very great. Thus, Robert Smith(1849) counted 450 on one limb and over 2000 on the whole body. Octerlong(1875) counted 2333 tumors on a negress of sixty-six years and the count did not include some of the smaller ones. But the record of patience in counting seems to be held by Hashimoto(1890), who made out 4503 tumors on the skin of a middle-aged Japanese man.

2. Distribution of Nerve Tumors. The distribution of nerve tumors on the body offers some matters of interest, especially in respect to symmetry and relation to particular nerves.

(*a*) *Symmetry*. Since the nerves of the body are symmetrically placed we might expect to find some symmetry in the distribution of nerve tumors, and such is often the case. Some authors specifically refer to such symmetry. For example, Speransky(1895) says the pea-sized tumors had a rather symmetrical distribution.

Sequeira(1916) states that his girl patient had symmetrical, bright red lesions on each side of the nose.

(*b*) *Distribution of Tumors among the Different Nerves.* The frequency with which the different nerves are mentioned in the reports might be expected to yield some facts of interest. But it has to be recognized that certain parts of the body are more apt to be seen and reported upon than others, because more accessible. Bearing this in mind the relative order of frequency with which particular nerves are mentioned is about as follows: ulnar, radial, orbital nerves, nerves of buttocks, sciatic and crural nerves. The various plexuses and the cranial nerves are often mentioned, but, on the other hand, the tumors are less common on the palmar surfaces of the hands and feet.

3. Symptoms Sometimes Associated with Multiple Neurofibromatosis. (*a*) *Scoliosis.* This is frequently mentioned, for example, by Genersich(1870), Speransky(1895), Antelme(1897), Adrian(1902), Lion and Gasne(1904), Chiray and Coryllos(1905), Hintz(1909), Oulmont et Haller(1909), Cole and Shawan(1911), Vignolo-Lutati(1911) and Rolleston and MacNaughton(1912). Sometimes the result is due to the formation of tumors on spinal nerves near their roots. Thus intervertebral ligaments are stretched and the verte- bral column distorted.

In the half-brother of Genersich's case (who also showed neurofibromatosis) the dorsal and lumbar regions of the spine were strongly bent backward and a little to the right without a compensatory forward bend. In Antelme's case there was a tumor on the left arm of such weight as to cause the patient's head and shoulder to bend toward the left and the thorax and even the spine and sternum to curve in. In Adrian's case a tumor on the right scapular region, of the size of the child's head, was removed at twenty-six years, and during the subsequent thirty years there had been a slowly increasing deformity of the spine and thorax. In Lion and Gasne's case a woman, aged forty-four years, who shows a few rather large tumors, has the thorax and vertebral column deformed in the sense of a dorsal kyphoscoliosis, with slight lumbar lordosis. In Chiray and Coryllos's case a man, aged thirty-seven years, who was improperly nourished in infancy, has now numerous fibromata and a very accentuated kyphoscoliosis. Eight of his 10 sibs died of meningitis in infancy. In Hintz's case a boy, aged five years, with numerous small swellings, a slight scoliosis, had been discovered at three years. In Oulmont and Haller's case a man, aged forty-nine years, had shown tumors since his tenth year, and they were now numerous and large. He was undeveloped mentally and sexually and showed a facial asymmetry and a slight scoliosis. In Cole and Shawan's case there are large tumors and a markedly deformed spine, but in this case there was a history of an injury

by being thrown from a wagon at twelve years. In Vignolo-Lutati's Case II the male patient, aged fifty-seven years, showed numerous small hard tumors, a slight lumbar scoliosis and a slight alveolar prognathism. In Rolleston and MacNaughton's case a girl, aged thirteen years, with incipient molluscous tumors, there was a slight scoliosis.

In considering these cases one must not forget that a slight scoliosis is rather common in the population at large, due to a variety of causes. Nevertheless, the relation of such scoliosis to tumors is in some cases (like Antelme's) direct and mechanical, in other cases probably due to less obvious relations to the formation of nerve tumors, such as swellings on the roots of the spinal nerves.

(*b*) *Sexual Impotence.* This is referred to, for the male, in several instances; for example, Hashimoto(1890), Chiray and Coryllos(1905), Deumié et Monéry(1908), Oulmont et Haller(1909) and Vignolo-Lutati(1911). The significance of this matter is not perfectly clear.

(*c*) *Feeble-mindedness.* While it is true that fibromatosis may occur in families showing the best of intellectual development, yet it is also true that the amount of feeble-minded among those who are affected with multiple neurofibromatosis is strikingly large. Of 243 persons described in the literature examined by us having multiple tumors, 19 were feeble-minded, or 7.8 per cent., or say twenty times the frequency found in the population at large.

4. Immediate Causes Stimulating the Development of the Tumors. It is often stated that the tumors develop in response to special stimuli. Thus in Labourverie's(1899) case the patient was a gendarme. The author states: "Irritation from sword-belt clothes, etc., and injuries have certainly contributed to the increase of certain tumors on the waist and back." A neuroma on the sciatic nerve is attributed to a strain resulting from jumping a ditch. However, one must not lay too much stress on these "explanations." Though tumors are frequent on the buttocks they are relatively rare on palms and soles. They sometimes arise about the region of the hat brim, but they also occur on the face, nose, jaw, popliteal space and in the nerves of the plexuses and the body cavity, where their development cannot be ascribed to special pressures. Very frequently they are numerous on the surface of the body before birth. No doubt pressure irritates tumors as they begin to form, but it is not the primary cause of tumor formation, and, indeed, it has little modifying effect.

5. Law of Recurrence of Neurofibromatosis in the Families. Multiple neurofibromatosis is a rare condition, as it is found in only about 1 in 2000 cases that present themselves to medical clinics or private practitioners for skin diseases. No doubt there are many abortive cases which never get into the literature, but,

even so, the proportion of the population which has the classical symptoms of neurofibromatosis is very small. Despite this there are many cases in the literature of two to six members of a family —blood relatives—who show some of the symptoms. Of such families the pedigrees of some are presented in Figs. 1 to 34. The frequent concurrence of these relatively rare symptoms in several

FIG. 1.—Front view of patient, M. G.

FIG. 2.—Rear view of patient, M. G.

members of one family cannot be accidental. It must be due either to the presence in the family of internal factors tending to induce the symptoms or to external agencies (such as contamination, germinal infection) which act upon individuals (like those of a family) who are in intimate contact. The fact that only *blood* relatives are affected speaks strongly against the contact hypothesis. The possibility of an infection through the germ cells cannot be

denied. It is to be noted, however, that father and child are quite as often affected in the same way as mother and child. This proves that the tumors do not belong to the class of diseases that are induced merely by infection through the placenta.

Though so many cases are on record of more than one affected person in a family, it is not to be overlooked that in very many reports no mention is made of relatives who have similar symptoms

FIG. 3.—Photomicrograph of section of characteristic neurofibroma in deeper layer of dermis taken from trunk. Magnification, 300 diameters.

with the patient; also, there are a number of cases in which the existence of affected relatives was denied. The charts given are of those of families in which there were two or more affected persons in one family. They represent only a few of the examples of such families studied by us in the literature.

In considering the nature of the family distribution we have first to recognize that the two sexes are apt to be affected in approximately equal numbers. Thus of the 243 persons described in the

literature examined as having multiple tumors there are 138 males and 105 females, or 56.79 per cent. males.

The disease tends to recur without a break in the generations, and it is nearly equally apt to be the case that the father or the mother of the patient is affected, whether that patient be male or female. Thus in the families charted we find that in the case of 119 males it is the father who is affected in 49 cases, the mother in 46 cases and neither parent is recorded as affected in 24 cases. In the case of

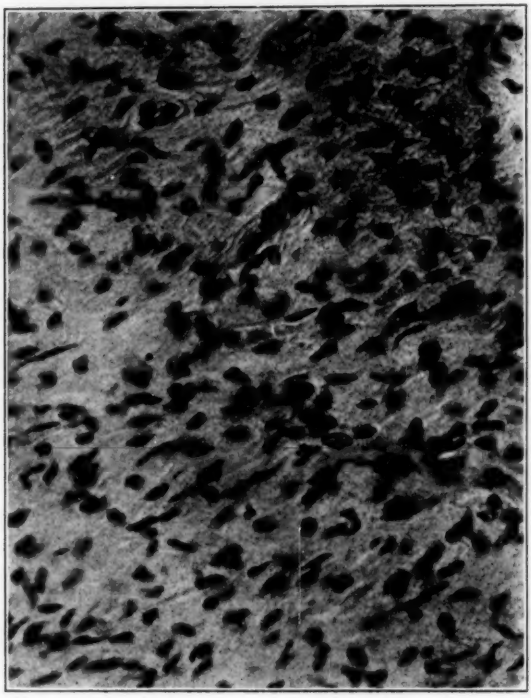

FIG. 4.—Same as Fig. 3, high power. Magnification, 700 diameters.

72 females the father is affected in 29 cases, the mother in 34 cases and neither parent is recorded as affected in 10 cases. We can here see no evidence of a difference in the distribution of the disease in the sexes when the father, on the one hand, or the mother on the other, is the affected parent.

In so many instances do the symptoms reappear in the direct line of ancestry that the hypothesis is at once suggested that the hereditary factor in neurofibromatosis is a dominant one. On this hypo-

thesis there is something in the germ plasm that positively facilitates the production, under appropriate stimulation, of tumors of the nerve sheaths.

On the hypothesis that neurofibromatosis depends on a dominant factor we should expect ordinarily half of the offspring of an affected parent to show the trait. Considering in the pedigree charts Nos. 7, 8, 10, 11, 12, 17, 18, 19, 21, 23, 24, 25, 26, 27, 29, 30, 31, 32, 33, 34 the fraternities with 2 or more offspring of an affected parent

FIG. 5.—Section of neurofibroma showing extensive degeneration. Magnification, 300 diameters.

we find (Table I) of 115 such offspring that 50 are affected. This is 43.5 per cent., approaching the 50 per cent. expected if there is a dominant factor for neurofibromatosis.

An apparent difficulty in the way of hypothesis that multiple neurofibromatosis is a dominant trait seems to lie in the fact that breaks in generations actually do occur. That "no family history" of a direct ancestor is obtained in response to the usual superficial inquiries made by the practitioner of hospital cases is not surprising;

the fact that a disease like his own occurs in other members of the family is apt to be denied (if indeed recalled) by the patient under the stressful conditions of the examination; the patient often exhibits the reactions of the malingerer. In a few histories like that of Fig. 29, II, 2, it seems probable that a generation is actually skipped. This is by no means fatal to the view that the disease depends upon a dominant trait, for a precisely similar result is obtained in experimental breeding of clear dominant traits, *e. g.*, in polydactylism of fowl. Occasionally a dominant trait simply fails of expression in an individual who carries it.

TABLE I.—PROPORTION OF FRATERNITY AFFECTED WITH NEUROFIBROMATOSIS.

No.	Total.	Affected.	No.	Total.	Affected.
7	2	2	26	2	2
8	7	2	27	8	1
10	4	3	29	8	3
11	2	2	29	5	2
12	11	1	29	6	1
17	6	4	29	3	0
18	2	2	30	3	1
19	3	1	31	5	5
21	4	3	31	5	0
21	2	1	32	2	1
23	3	3	33	5	1
24	3	1	33	7	3
25	3	1	34	4	4
		Totals		115	50

6. Special Family Types. In examining comparatively the symptoms shown by different patients one finds a great diversity in them, and also that the special symptoms exhibited in one member of the family are very like those shown in another member. The resemblances relate to the region preëminently affected, to the nature of the tumors, to the time of their development and so on. Let us consider some examples of these family resemblances in symptoms.

(*a*) *Family Resemblances in Location of Principal Tumors.* Since in most cases the tumors are exceedingly numerous it is to be expected that they will sometimes occur in different members of the family in corresponding parts of the body. But, apart from this, we have instances in which single exceptional tumors appear in exactly corresponding places, and this frequency must be regarded as significant. Some of these instances are here cited from the appendix.

Bruns(1870). The patient was born with a flat tumor of the left temple and left upper eyelid which grew with the growth of his body into a lobed sac hanging over the (not atrophied) eyeball. His brother had a tumor of the temporal region and the left upper

eyelid almost exactly like that of his brother, and which grew in the same way.

Genersich(1870). The patient has numerous small tumors, but on the upper part of the right buttock there is a soft lipoma the size of two fists. His half-brother had at ten weeks before his death a tumor the size of a fist in the deep part of the buttock. It grew very rapidly and at the time of his death was seventeen inches in circumference.

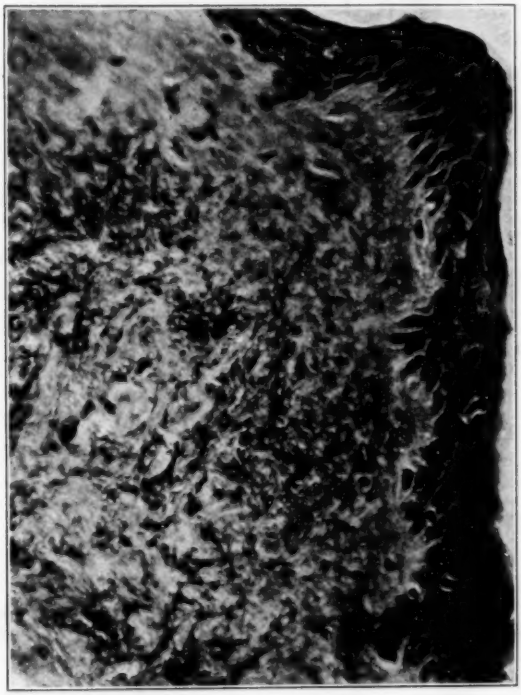

FIG. 6.—Same as Fig. 5, high power. Magnification, 700 diameters.

Murray(1873). In the patient, aged seven years, the last phalanx of the fingers, with one exception, and several of the toes, were hypertrophied to from three to four times their natural size. A four-year old sib had the end of one of the fingers similarly enlarged. In the patient the gums were greatly hypertrophied, covering up almost entirely the teeth. The two younger sibs presented the enlarged gums.

Czerny(1874). The patient is said to have been born with a

small swelling on the back; at six years a physician certified that it was as large as a fist; at twenty-five years it hung down so far, starting from the region of the lowest thoracic vertebræ, that she

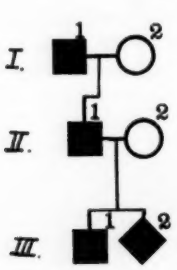

Fig. 7

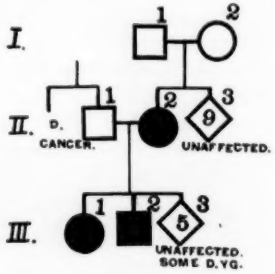

Fig. 8

Fig. 7.—Case of R. Virchow, 1847. III 1, patient had numerous knotty soft fibroid tumors. III 2, similarly affected sibs; number and sex unknown. II 1, similarly affected father. I 1, similarly affected grandfather.

Fig. 8.—Case of A. Hitchcock, 1862. III 2, propositus, aged forty-six years, showed numerous small pedunculated skin tumors; a large one of twenty years' standing lay on the ulnar nerve; this returned after removal. III 1, a sister, began to have tumors at ten years. After removal of tumors numerous others arose. II 1, had brothers and cousins who died of cancer. II 2, at eighty-one, had hundreds of tumors, which grew slowly in number and size; she denies that her sibs or parents had tumors.

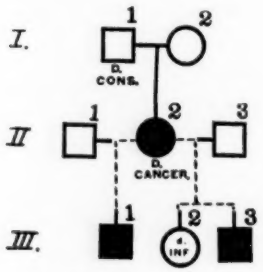

Fig. 9

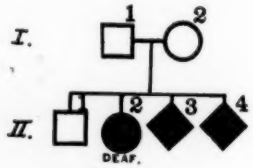

Fig. 10

Fig. 9.—Case of A. Genersich, 1870. III 1, a day laborer, aged thirty-four years, showed numerous hard and soft skin tumors; on autopsy many fusiform tumors were found upon the nerves. III 3, a half-brother, showed numerous resistant, fusiform tumors which were first noticed at eight years; on autopsy fibromata and also sarcomata were found on numerous nerves. II 2, died of cancer of the breast; she had small cancers on nerve trunks.

Fig. 10.—Case of J. Murray, 1873. II 2, aged seven years, showed a variety of cutaneous growths; some of the tumors grew again after removal. II 3, 4, children of four and two years, who show beginnings of tumors. I 1, 2, first cousins; showed no tumors.

was obliged to give up her field work. Her mother had a tumor in the region of the upper thoracic vertebræ like that of her daughter; when it was extirpated it weighed 38 pounds. The

mother's brother had a tumor on his back which hung down so as almost to prevent his walking; the mother's father had a similar

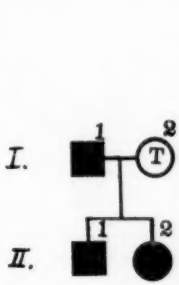

Fig. 11

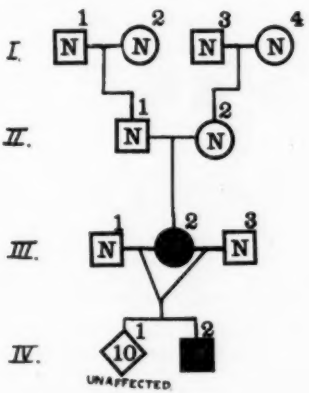

Fig. 12

Fig. 11.—Case of J. E. Atkinson, 1875. II 1, Timothy Lyons, aged fifty-six years, shows multitudes of small tumors, some 5 cm. in diameter; has large pigmented nevi verrucosi. II 2, aged fifty years, fewer tumors than brother, with a tendency to pedunculation; present since infancy. I 1, had numerous tumors; one "weighed two pounds."

Fig. 12.—Case of Octerlony, 1875. III 2, patient, a negress, aged sixty-six years, showed 2333 skin fibroid tumors of varied size and consistency. IV 2, of eleven children, one at twenty-two years, had numerous tumors. II 1, 2, parents, as well as grandparents, said to be unaffected.

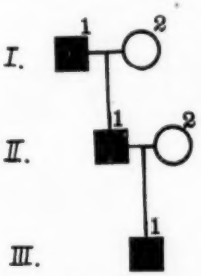

Fig. 13

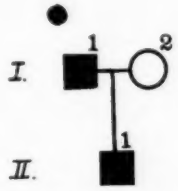

Fig. 14

Fig. 13.—Case 1 of T. Fox and T. Farquhar, 1876. III 1, a Brahmin, aged thirty-three years, showed from adolescence numerous small skin tumors, now of varied size and consistency. II 1, at sixteen years, began to show numerous small skin tumors. II 2, unaffected. I 1, had numerous tumors, mostly about the size of a pea.

Fig. 14.—Case 6 of Fox and Farquhar, 1876. II 1, aged sixty years, has had body studded with tumors from childhood if not from birth; one is now as large as an orange and cystic in consisteney. I 1, similarly affected.

huge swelling on his left arm. The mother's father's brother had a swelling on his back which hung far down and almost prevented

his walking. Thus in three generations there was the tendency to form a huge tumor, usually on the thoracic vertebræ.

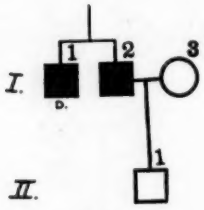

FIG. 15

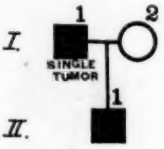

FIG. 16

FIG. 15.—Case of Fox and Farquhar, 1876. I 2, a Mohammedan coolie, aged forty-five years, shows numerous sessile tumors of various sizes. His son, II 1, aged thirteen years, is still free from tumors. I 1, affected like his brother; his parents unknown.

FIG. 16.—Case 8 of Fox and Farquhar, 1876. II 1, an East Indian boatman, aged thirty-five years, had tumors from childhood, which constantly increased in number and size. A huge tumor, which felt like a half-filled bladder, was excised, but after eighteen months grew more rapidly than ever. I 1, had a single tumor over the left shoulder-blade.

Herczel(1890). After describing in detail the distribution of tumors in the patient, states of the mother, who had tumors also, that "these growths are in exactly the same places as in the daughter."

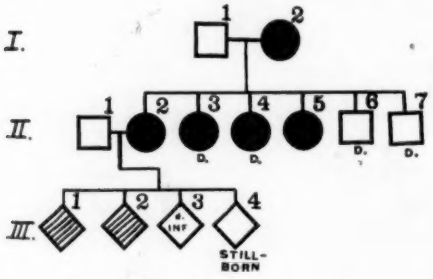

FIG. 17

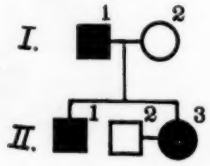

FIG. 18

FIG. 17.—Case of Konigsdorf, 1899. II 2, aged forty-five years, showed over 600 skin tumors of varied size, with golden pigment spots and increasing scoliosis. Autopsy revealed numerous soft fibromata of the skin, throat and liver, fibrosis of the dura mater and lipoma of the left kidney. II 3, 5, three sisters had tumors like her own. I 2, had tumors like the patient's.

FIG. 18.—Case of Hashimoto, 1890. II 1, a Japanese, aged forty-two years, was born with skin tumors which have increased in number to 4503, of varied size; the skin is also pigmented. II 3, has fibromata over her whole body. I 1, had numerous skin tumors.

Moses(1890) records the case of a man with multiple tumors that produced an elephantiasis. The mother had the same affection of soft multiple fibromatosis and elephantiasis as the son.

In Rapok's(1890) case, father and daughter had a plexiform neuroma. In Phillipson's(1893) case, mother and mother's mother had a fibroma in the inguinal furrow, and the daughter had one in

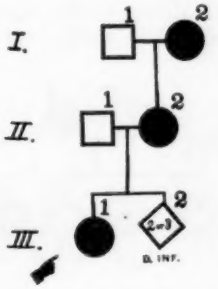

FIG. 19

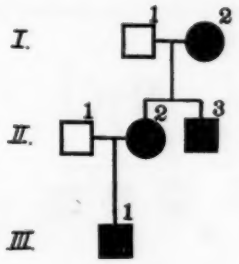

FIG. 20

FIG. 19.—Case of J. C. Gilchrist, 1896. III 1, aged twenty-six years, has had tumors all her life; shows a violaceous patch and a telangiectatic spot. Five days after removal a tumor was replaced by a sarcomatous growth. II 2, died at twenty-five years, with an enormous number of tumors, some of great size, one of which developed into a cancer. I 2, affected like III 1.

FIG. 20.—Case of W. Menke, 1898. III 1, aged twenty-three years, shows innumerable pigment spots and numerous neurofibromata. II 2, has neuroma; a large one in the same place as her son's large tumor. II 3, had numerous small tumors on his arms from birth. I 2, had small nodules along the nerve tracts of all extremities.

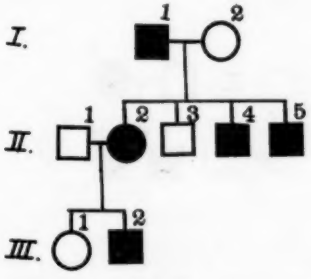

FIG. 21

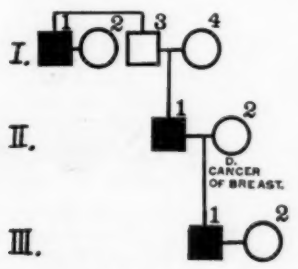

FIG. 22

FIG. 21.—Case of T. Carwardine, 1899. III 2, aged twenty-five years, was covered with nodules of varied size, some deep-seated, and a pendulous fibroma upon one buttock. Several pigment patches and a multitude of freckles. II 2, similarly affected. II 4, 5, similarly affected. I 1, similarly affected.

FIG. 22.—Case of J. Labouverie, 1899. III 1, gendarme, aged thirty-four years, shows numerous brown punctiform spots; four cutaneous fibromata, a molluscum fibrosum and a molluscum pendulum on the back. Tumors at the waist exaggerated by sword-belt. II 1, aged fifty-six years, showed patches and numerous fibromata of the nerves. I 1, aged eighty-eight years, showed pigment patches and molluscous tumors.

the "genital region." Gilchrist(1896) reports on the similarity of the growths in daughter, mother and mother's mother. Tailhefer (1897) emphasizes the similarity of the tumors in the patient, her

sister and father; and Spillman et Etienne(1898) find similar or exactly similar tumors in son, mother and mother's father. Bourcy and Laignel-Lavastine(1900) find three generations of scalp tumors.

In Malherbe's(1901) case, mother and daughter had exactly similar tumors on the left breast. In Menke's(1898) case the tumors in three generations are large ones on the median nerve; in

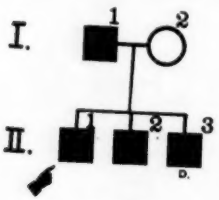

FIG. 23

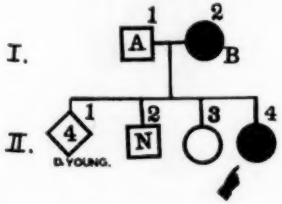

FIG. 24

FIG. 23.—Case of B. G. A. Moynihan, 1901. II 1, aged thirty-seven years, showed whole body covered with small tumors, some sessile and some pedunculate. Irregular pigment patches were shown which, like the excrescences, were present at birth. One tumor, taken from the vagus, proved to be a neurofibroma. II 2, 3, covered with brown patches and soft excrescences. I 1, like his sons, covered with patches and soft excrescences.

FIG. 24.—Case of C. Adrian, 1902. II 4, was subject to cutaneous tumors from birth on. At fifty-six years they were very numerous, sessile and pedunculate; brown skin patches were present. On autopsy neurofibroma were found on the viscera. I 2, had numerous tumors over the surface of the body; became blind, "B."

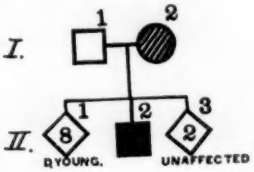

FIG. 25

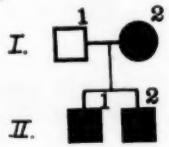

FIG. 26

FIG. 25.—Case of Chiray and Coryllos, 1905. II 2, aged thirty-seven years, showed pigmented spots from birth; tumors from twenty years. Fibromata are specially marked on superficial nerves of the appendages. I 2, has pigmentation like son, but no tumors.

FIG. 26.—Case of C. R. Keyser, 1905. II 1, aged thirty-eight years, shows numerous painless skin tumors gradually becoming more numerous; there are large pigmented areas. II 2, even more markedly affected by multiple tumors. I 2, said to have died of tumors which formed a large growth extending across her chest.

Thomson's(1900) case one of the striking tumors occurs in father and son on the buttocks; in de Haam's(1912) case there are two generations of swelling over the eye. In Lange's(1906) case the family showed a stronger tendency to form pigment patches than tumors, while in other cases no pigment patches are seen. In Du Bois's(1917) case mother and daughter had a large tumor arising from below the left breast.

The foregoing examples illustrate the conclusion that not only is there a general tendency to multiple tumors in the family but also a tendency to produce them of the same type and in the same places.

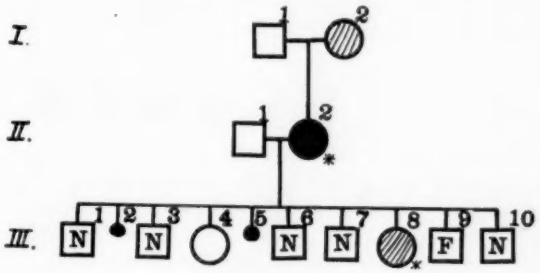

FIG. 27

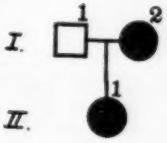

FIG. 28

FIG. 27.—Case of E. B. Meek, 1905. II 2, aged forty years, shows numerous subcuticular nodules which are painful; also pigment spots. The optic nerve is beginning to atrophy. III 8, shows numerous pigment spots but no tumors. I 2, had pigment spots in the skin. *Individuals seen by Meek.

FIG. 28.—Case 1 of F. Harbitz, 1909. I 2, aged fifty-two years, showed numerous fibromata and pigment spots. II 1, aged twenty-three years, showed pigment spots, angiomata and soft fibromata.

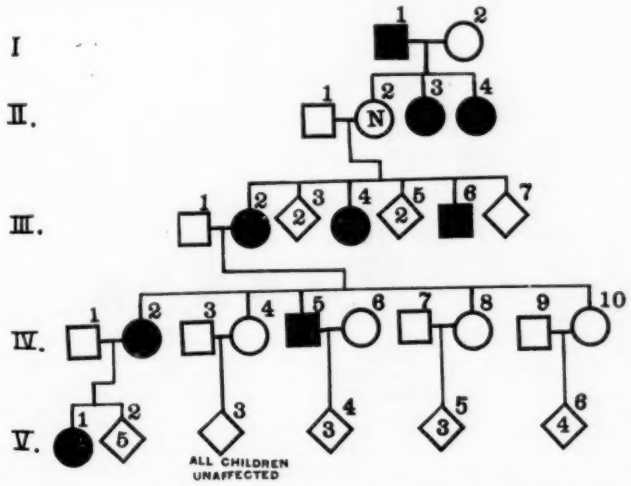

FIG. 29.—Case 9 of F. Harbitz, 1909. V 1, aged twenty-five years, showed "elephantiasis" of the left leg, due to confluence of fibromata. Similar "elephantiasis" had existed in other members of the family, as shown on the chart.

(*b*) *Family Resemblances in the Associated Symptoms.* Inside a particular family the symptoms often show special idiosyncrasies. The behavior of the *pigmentation* in families is peculiar. Some-

times it will be only the pigmentation changes that are shown by a young child of an affected person; in such a case one suspects that

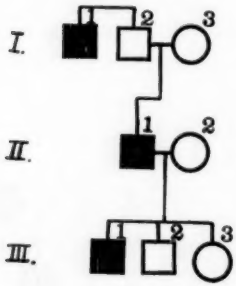

FIG. 30

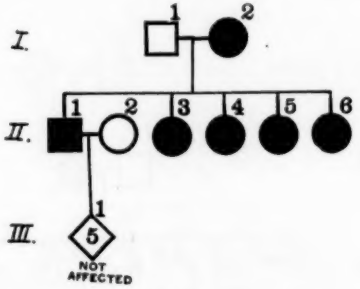

FIG. 31

FIG. 30.—Case of A. Hintz, 1909. III 1, aged five years, showed numerous gold-brown flecks and numerous little swellings beneath the skin. III 2, showed a red mark on the body. II 1, aged forty-two years, showed small skin tumors by the thousand; some sessile and some pedunculate. He had also flecks of pigment. I 1, had skin changes like his nephew.

FIG. 31.—Case of H. M. Cole and H. Shawan, 1911. II 1, aged forty years, showed multiple subcutaneous tumors from boyhood; the skin shows pigment blotches. II 3–6, all have multiple skin tumors. I 2, had a round painless tumor removed from her arm; no multiple subcutaneous tumors.

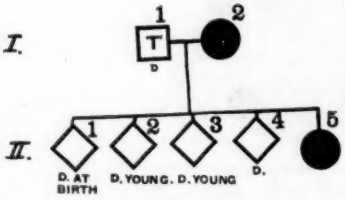

FIG. 32

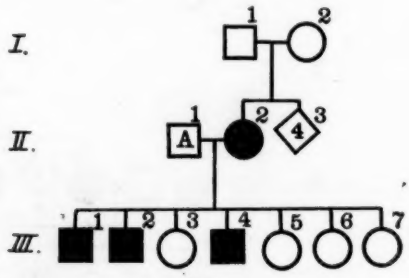

FIG. 33

FIG. 32.—Case of W. B. Trimble, 1911. I 2, aged forty-seven years, was practically covered with small fibrous tumors, varying in size and color; also with areas of skin pigmentation. II 5, aged nineteen years, has small tumors on her arm which first appeared at sixteen years.

FIG. 33.—Case of A. Mathies, 1913. II 2, aged thirty-five years, died blind and deaf. Autopsy showed numerous tumors along peripheral nerves, tumor of the orbit, knots at base of the brain, tumor of optic chiasma and visceral nerves. III 1, aged fifteen years, blind and deaf on left side, numerous tumors along peripheral nerves. III 2, aged thirteen years, undeveloped, tumor of the twelfth cranial nerve on a cutaneous posterior femoralis. III 4, aged twelve years, undeveloped, many tumors on arm.

the tumors will appear later. In other cases, however, the parent of an affected person may show pigment only—no tumors. However, in many cases the pigment relations are similar in various

members of the family. For example, extensive pigmentation of patient and mother is noted in the Herczel(1890) case. In Salomon's(1878) case the small coffee-colored flecks were alike in brother and sister. Spillman et Etiene(1898) report a case with pigment patches in two generations and one case without patches in two generations. Sutherland(1906) reports similar pigment spots in three generations.

The size of the tumors is usually variable. Frequently a single or a few large tumors appear. There is a notable case described by Czerny(1874), such as one might doubt if we had to do with multiple fibromatosis were there not numerous small tumors, though no pigment changes. On the other hand in not a few families, such as those of Fox and Farquhar(1876), the tumors are all small.

A tendency to produce the rather uncommon *confluent tumors* (elephantiasis) also runs in families. In Moses's(1890) case mother and son showed "elephantiasis." In Harbitz's(1909) case No. 2 elephantiasis appeared in five generations.

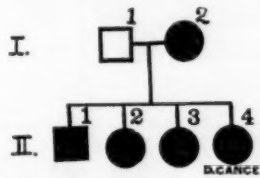

FIG. 34.—Case of Billington, 1914. II 1, aged thirty-seven years, showed superficial tumors all over the body from childhood. II 2, 3, had many subcutaneous tumors. II 4, had growths all over the body; died of cancer. I 2, had a tumor on the right arm.

Finally, though the tumors are usually benign, yet in some families they tend to *develop into sarcomata*. For example, in Arnozan and Prioleau's(1883) case a tumor in the patient was tending into a sarcoma and a sister's large tumor was sarcomatous. In Genersich's(1870) family some of Karl's tumors were distinctly sarcomatous and in his mother, tumors and cancers were intermingled. Even the specific method of tumor growth may be characteristic of a family. Thus in a family described by Hitchcock(1862) the tumors have the remarkable habit, throughout the family, of speeding up in middle age.

It seems probable that the precise nature of the symptoms shown in any case of neurofibromata is determined in large part, if not chiefly, by constitutional factors, and that in symptomatology of multiple neurofibromatosis, as in that of so many other diseases, we may distinguish biotypes—that is, family hereditary differences that are due to the specificity of the different germ plasms.

7. OTHER MULTIPLE TUMORS THAT ARE INHERITED IN THE SAME WAY AS NEUROFIBROMATA. There are many cases of formation of

multiple tumors that are perhaps related to multiple fibromatosis. Such, for example, is the group of telangiectases and polyadenomata.

(*a*) *Multiple Telangiectases.* This is a tendency to form vascular tumors in the skin and mucous membranes. These are sometimes hemispherical; at other times they have a "spider form;" in the latter type they are often associated with epistaxis. Examples are cited by Osler(1907), and numerous observers agree that the tendency recurs in successive generations, without skipping, and usually about half of the children of an affected parent are affected. This shows that the tendency to multiple telangiectasis is a dominant trait in heredity.

(*b*) *Polyadenomata of the Rectum.* Oidtmann(1917) has encountered 8 cases of polyadenomata of the rectum. Six of the patients belonged to two families, 3 sisters in one family, and mother, son and daughter in the other. References are given to nine other families showing from 2 to 6 cases, each of polyadenomatosis. A cancerous tendency is often present.

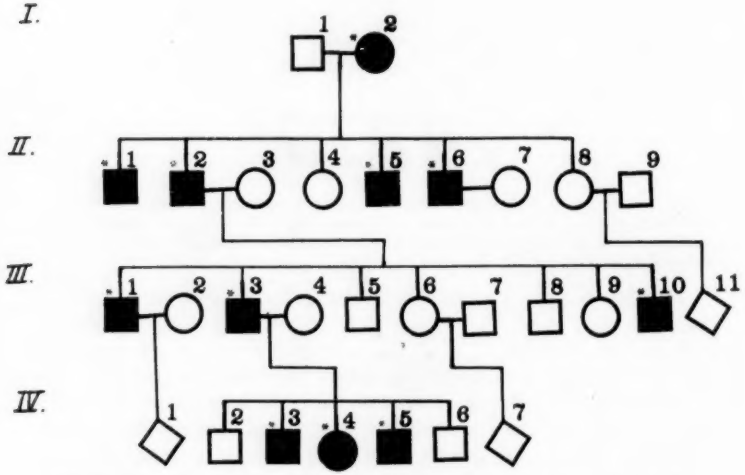

FIG. 35.—Pedigree chart of Blumer's (1892) family showing epidermolysis bullosa in four generations. Affected individuals are indicated by black symbols. The asterisk (*) indicates that the individuals were seen by Blumer.

Multiple fibromatosis, multiple telangiectasis and polyadenomata are the three classes of tumors (or tumor-like swellings) of which the inheritance has been carefully studied. It is remarkable that in all, inheritance seems to be of the simple dominant type, which we may interpret to mean that the tendency to form numerous "benign" tumors is due to some positive factor or to the presence of some unusual condition or substance that causes the rare reaction.

So, likewise, the tendency to form pigment patches in the skin—ephelides—is a dominant one, as Hammer has found.

Not only the tendency to form multiple tumors but numerous other skin troubles also are inherited as dominant traits. Examples of an inherited tendency to form bullæ or large edematous patches are: epidermolysis bullosa (Fig. 35), angioneurotic edema (Fig. 36) and persistent hereditary edema. Moreover, the diverse skin modifications seen in psoriasis, porokeratosis and ichthyosis have a positive hereditary basis, and ordinarily do not skip generations. Just what the usual dominance of all these abnormal skin conditions means (if it is anything other than chance) is quite obscure.

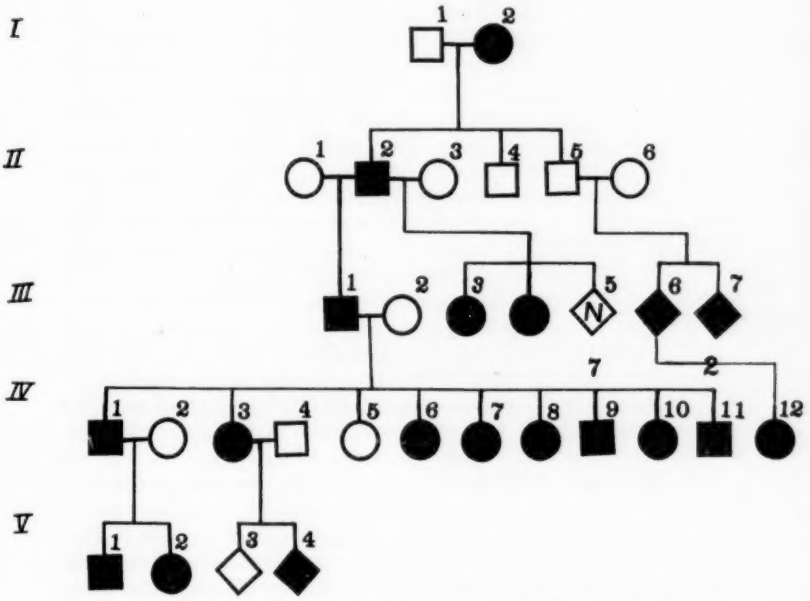

FIG. 36.—Pedigree chart of Osler's (1888) family, showing angioneurotic edema in five generations. Affected individuals are indicated by black symbols.

8. RELATION OF NERVE TUMORS TO CANCER. The tumors that we have been considering are mostly "benign." That is to say, they usually grow slowly and frequently cause no special inconvenience. If let alone they may remain as small as hazelnut-sized swellings until death intervenes at an advanced age. In some cases the tumor becomes larger and pendulous and the owner seeks to have it removed. Operations for this purpose have often been performed without recurrence of growth, at least for months, *e. g.*, Hitchcock(1862). On the other hand surgical interference is fre-

quently followed by regrowth, sometimes a sarcomatous growth of tissue at the point of removal of the tumor. As an example of the regrowth of a tumor we have Czerny's(1874) case, in which a part of a large tumor was removed, but the tumor continued to grow. In Hartmann's(1896) case a tumor on the crural nerve was removed but a new tumor quickly developed. As examples of sarcomatous growth we have Gilchrist's(1896) case, in which a removed tumor was replaced within five days by a sarcomatous growth, the mother of the patient having had tumors and a cancer. Also Barse's(1917) case, where, after removal of the tumor, the growth "then took on a very malignant course and recurred with startling rapidity; a microscopic examination of a portion of the tumor showed it to be a small spindle-celled sarcoma."

The nerve tumors are often of a sarcomatous nature. Thus in Adrian's(1901) case the largest tumor was a fibro-myxo-sarcoma, while the other skin tumors showed the typical structure of neurofibromata. In Adrian's(1902) case, which showed multiple fibromata of the skin and viscera, the neurofibroma of the duodenum underwent sarcomatous degeneration. In Mathies's(1913) case there were tumors on the cranial and spinal nerves and "myxofibrosarcomata" of the peripheral nerves. Genersich(1870) also found, on microscopic examination, some of the tumors to be essentially fibromata, but some were distinctly sarcomatous and others myxomatous. Wedge-shaped masses in the lungs were sarcomatous.

9. Bearing of Foregoing Facts on Heredity of Cancer. It is, of course, only in accord with common observation that tumors may develop into sarcomata or other malignant types of growth. The fact that multiple fibroneuromata do so bears on the question of "heredity of cancer," which is so much discussed.

This question is a perennial one. Of late it has come to the fore because of the doubt cast upon heredity of cancer by life insurance actuaries and statisticians using the method of mass statistics. On the other hand new evidence for the inheritance of cancer has come from the experimental pathologists who all agree that in mice there are strains that cannot grow cancers and others in which they grow rapidly. The hereditary behavior of such strains has even been investigated experimentally by Tyzzer and Little. Now the cancers of mice are so entirely like those of man that it is extremely probable that if the one has an hereditary basis the other has also.

Another reason for the view that cancer is hereditary is that there are races of men who are almost immune to cancers, such as the American Indian, full-blooded negroes and some aborigines of Australia and the Pacific Islands. Also, there are racial peculiarities in the organs affected by cancer; among the Japanese women cancer of the generative organs is about as common as in Great

Britain, but cancer of the breast only one-tenth as common. Also, we cannot overlook the significance of such facts as that of the occurrence of sarcoma of the eyeball in three generations in the direct line and four individuals of the middle generation of this family (Silcox 1892).

Finally, the fact of cancer villages, where there has been much intermarriage, is strong additional evidence of the racial significance of liability to cancer. In view of all these considerations we must consider the presence of an inheritable factor in cancer as practically certain. But we are, nevertheless, very far from a knowledge of the law of its inheritableness. That is a matter for future investigation.

10. Pathology of the Disease. There is a great deal of discussion regarding the pathology. It was in 1881 that von Recklinghausen(1882) called attention to the frequency of the association of multiple neuromas and cutaneous fibromas. He termed these latter neurofibromas, but later (1898), holding that the essential feature was an overgrowth of the connective-tissue envelope of the nerve bundles and of the endoneurium, and that the term neuroma should be restricted to tumors formed of proliferative nerve cells, he concluded that the tumors of this disease should be placed among the fibromata.

Knauss(1898) has described an instance in a girl, aged eleven years, of multiple subcutaneous growths of this order in which he discovered abundant ganglion cells.

The consensus of opinion seems to be that the tumor is neither a neuroma nor a glioma, but according to Adami(1911) a neurinoma or neurofibroma. "We deal with a condition of neuromatosis; the multiple nature of the growths along the continuity of the nerves demonstrates this. What is of interest in this connection is that in a large number of cases a study of the central nervous system showed the coincident existence of gliomatous areas in the brain and spinal cord. We deal with a tendency toward excessive vegetative activity of the nervous tissue, and where the condition affects the sympathetic ganglia there may develop true neuromas."

These tumors are to be differentiated from gummata, sarcomata, lepra and tuberculous nodules; but a careful inspection usually, and the microscopic examination always, will separate these conditions from the one under discussion.

The neurofibromata are slowly growing tumors of benign nature. Frequently they undergo a retrograde metamorphosis and show cystic, fatty or myxomatous degeneration. In some instances these tumors undergo sarcomatous transformation, assuming a malignant character, rarely then giving rise to metastases.

11. Description of the New Case. Case I.—M. G., aged forty-five years; male; born in Austria; peddler by occupation;

married; admitted to Montefiore Home and Hospital December 11, 1915; died September 29, 1916.

Family History. Father died at seventy-eight years, cause unknown. Mother alive and well. Negative for tuberculosis and cancer. No history of any degenerative disease in the family.

Personal History. Patient was always one of good habits, attended school, stating that he had never had any particular difficulties in his studies. Patient's first occupation was that of a painter, which he had to discontinue because he developed lead poisoning. He then became a peddler, continuing this occupation until a few months before admission to the hospital. He married at the age of twenty-five and his wife gave birth to eight children. The oldest has von Recklinghausen's disease and is mentally defective, and another child suffers from Hirschsprung's disease. (This child has since died.)

Past History. No diseases of childhood. No pneumonia, malaria, typhoid or rheumatism. Twelve years ago he was in Bellevue Hospital for two months, suffering from painter's colic. Eleven years ago he was operated upon in Bellevue Hospital for a tumor of the shoulder and neck, which had existed for one year.

Present Illness. This began twelve years ago. Soon after the attack of painter's colic he noticed the appearance of pigmented spots and of small tumor masses over the body. During this time he suffered from very frequent attacks of headaches, dizziness, palpitation and pain about the heart, at times associated with vomiting. The dizziness was frequently associated with staggering, so that, while walking, he was often falsely accused of drunkenness. Hearing of right ear impaired for six years. Vision of both eyes poor for the past five years. Attempts at reading a paper result in dizziness. No other organic disturbances. Has been in Mt. Sinai Hospital four times during the past eight years for the above complaints. The last time was two years ago.

For the past six months had headaches, with dizziness, pains about heart, with palpitation; pains all over body have become markedly aggravated. Of late he has also noted edema of lids and of the ankles, increasing during the day when up and about. During these six months has coughed a great deal, with mucoid expectoration, and has lost twenty-five pounds in weight.

Status on Admission. Patient is an adult male, poorly nourished, confined to bed and appears to be suffering from a chronic illness. Mental condition shows no evidence of inferiority or degeneration. The entire body, with the exception of the palms of the hands and the plantar surfaces of the feet, is covered with numerous pigmented areas varying in color from a light to a dark brown, confluent in the region of the neck. Nevi are present here and there and vary in size from a circular patch of one-sixteenth of an inch to an irregular-shaped nevus an inch or more in diameter. The

nodular elevations are in the main sessile, but a lobulated mass is present in the right temporal region (fibroma molluscum) and a pedunculated one in the region of the upper dorsal vertebræ. The masses vary in size from one-eighth of an inch to one inch. They are mostly soft, but a few hard ones are present here and there. The former are painful when squeezed between the fingers. The head is symmetrical and covered with an abundance of dry, dark brown hair.

Eyes. Conjunctivæ injected. Von Graefe's sign present. Pupils are equal, regular and react to light but poorly in accommodation. No nystagmus. Arcus senilis present in both eyes.

Ears and Mastoids. Externally negative. Hears watch with right ear at three inches, with left at fifteen inches.

Buccal Cavity. Mucous membranes of good color. Teeth in poor condition. No pyorrhea. Tongue protrudes in median line; fine tremor present.

Neck. Symmetrical, rather long and thin. No abnormal pulsations visible. The cervical vertebræ are freely movable and there is good mobility of the entire vertebral column.

There is a very marked crepitation of the right shoulder on passive motion; less crepitation in the left. Patient complains of pain on moving the shoulder; no tenderness; no effusion in the joint. The muscles of the finger-joints are very hypotonic, especially those of the left hand. There are slight Heberden nodes in the small joints of the first, second, third and fourth fingers of the left hand and all the fingers of the right hand.

Both knee-joints crepitate. The ankle-joints appear normal The joints of the toes also appear slightly hypotonic. No restriction of mobility of the knee-joints. The terminal phalanges of the fingers appear to be broader and shorter than usual. The epitrochlear glands are enlarged on the right side. Numerous rather small axillary lymph nodes. The inguinals are slightly increased.

Chest. Expansion poor, somewhat diminished on the right side. Respiration labored and accelerated. Supra- and infraclavicular retraction on both sides. Percussion note is hyperresonant and anteriorly except over a small area of precordial dulness. Over the whole chest expiration and inspiration are prolonged, expiration being of a higher pitch than inspiration. There are fine crepitant rales scattered over the whole chest, but they are more numerous over the right side. Posteriorly there is a hyperresonant note in both infrascapular regions. Respiratory murmur is emphysematous in character, with scattered fine rales from apex to base all over the chest.

Heart. Upper border is at the third space. Right border measured in the fourth space is at the right sternal border. Left border, in the fourth space, is 10 cm. from the median line. Apex

beat not visible or palpable; heard in the fifth space within the nipple line. Sounds are distant, regular, of good force; no murmurs. Radials are equal, regular, good force; vessels are thickened and slightly tortuous. Heart action is rather slow, 60 per minute. (This was not changed during the disease.)

Abdomen. Symmetrical; no signs of fluid; no distention. Liver, spleen and kidneys are not palpable. Slightly tender and very indefinite mass in the left hypochondrium.

Reflexes. Knee-jerks and Achilles and abdominal reflexes are exaggerated.

Sensation. Normal.

Fundi. Normal.

Blood-pressure. Systolic 115, diastolic 90.

Polygraphic tracings of the heart were normal.

Blood. Hemoglobin, 85 per cent.; red blood cells, 3,950,000; white blood cells, 13,800.

Differential White Blood Count. Neutrophiles, 84 per cent.; lymphocytes, 14 per cent.; large mononuclears, 1 per cent.; eosinophiles, 1 per cent. The eosinophile count, which in some cases of von Recklinghausen's disease, according to Galliard, runs as high as 15 per cent., was not raised in this patient.

Urine Examination. Light amber; acid in reaction. Specific gravity, 1010; albumin negative; sugar negative. Microscopic examination negative, except for a large amount of urates. Melanin negative.

Sputum Examination. Only once positive for tubercle bacilli.

Wassermann Reaction of Blood. Negative.

Roentgen-ray Examination. Chest. Marked infiltration of right upper lobe and inner portion of right lower lobes. Evidence of extensive adhesions at the median portions of the diaphragm on both sides. A number of dilated bronchi around both roots. Ascending aorta slightly dilated, showing abnormal pulsation.

Skull. Marked rarefaction of frontal bone. Faint outlines of anterior and posterior clinoid processes (softening). Sella turcica itself normal in size and shape.

Spine. Slight scoliosis of upper dorsal spine to left; of lower dorsal spine to right. No roentgen evidence of any other pathological change.

Hands. Bony excrescences at the bases of all the end phalanges. Moderate broadening of the basal portions of the middle phalanges of the second and fifth fingers. No arthritic changes in the bony parts of any of the joints.

Diagnosis. The diagnosis was obvious and was made on first examination. The patient was put on thyroid and suprarenin extract, with no effect. He was examined at short intervals and was noticeably becoming gradually weaker and weaker and the pigmentation more marked, especially around the neck, pectoral

region and abdomen. After some nine months' stay in the hospital he finally died of general asthenia.

Autopsy. The autopsy findings of the abdominal viscera proved negative, with the exception of the pigmentation in the liver and spleen. The examination of all the ductless glands as well as of the brain revealed nothing of note. There was evidence of chronic tuberculosis in the lungs.

Microscopic Sections. Microscopic sections were made by Dr. B. S. Klein, pathologist of the Montefiore Hospital, to whom we are indebted for the following description:

Skin. Section 1. In the subcutaneous tissue there is an area equal to several low-power fields, quite sharply marked off from the surrounding tissue. This area resembles nerve tissue throughout. In the lower layer of cells of the epidermis overlying there is a considerable amount of brown pigment. In the dermis a little below these latter cells there are a number of flat polygonal cells, with numerous brown granules in the cytoplasm. In a few places small extracellular clumps of brown granules are seen. In a few places in the subcutaneous nodule the elongated nuclei are less numerous than elsewhere, the cytoplasm of the cells is more prominent than elsewhere and has a more homogeneous structure. In the skin for some distance from the tumor the cells of the deeper layer of the epidermis and a number of cells in the dermis show a moderate to considerable amount of small brown granules. In another area of the section there is a nodule similar in appearance to the one described above, occupying an area less than a low-power field. Throughout the section the dermis is more dense in structure than normal; in many places the nuclei are fewer than normal; the tissue has a homogeneous uniformly pink-stained appearance, suggesting beginning hyalinization. Scattered throughout the nodule there are new-formed capillaries in fair abundance, most of them dilated. In the outer layers of the dermis, near the Malpighian layer, the tissue is quite structureless and in places has a stringy, bluish appearance. There are all stages between this appearance and that of the tissue suggesting nerve fibers, including a structureless, homogeneous pink-stained tissue. Scattered throughout the tumor are very many mononuclear eosinophilic cells not associated with other round cells and suggesting fixed tissue cells.

Section 2. Shows an area in the subcutaneous tissue larger than a low-power field fairly well circumscribed. The structure of this nodule is much denser than the one described above; in great part the tissue has a stringy blue-stained appearance and is homogeneous. Throughout this tumor and in the overlying dermis the bloodvessels are very tiny as compared with the vessels in corresponding areas in the tumor above described. In the dermis and epidermis overlying this tumor the pigmentation of the cells is much more intense. The latter tumor is apparently undergoing

degenerative change. There is also much homogeneous pink-stained tissue throughout.

Section 3. Shows throughout the section numerous brown granules in the cells of the deeper layers of the epidermis and of the scattered cells in the dermis. The portion of the dermis adjoining the epidermis is more dense in structure than normal. In places the tissue has a dense homogeneous pink-stained appearance, suggesting beginning hyalinization. Section of a nerve in the vicinity of these nodules shows at one place an accumulation of small mononuclear cells about a small vessel. The fibers show no apparent change.

Lungs. Section 1 shows the greater number of the alveoli and bronchioles filled with exudate. In the majority of places there are many polymorphonuclear leukocytes, a moderate number of mononuclear cells; some of these with engulfed blood pigment and débris, a varying number of red cells and a varying amount of serum. In places there is a fair amount of fibrin. The exudation is not uniform throughout; in places the spaces contain serum, a few desquamated cells and a few wandering cells. There are all gradations between alveoli of this character and those in which they are packed with polymorphonuclear leukocytes. The alveolar vessels throughout are moderately engorged. The exudate nowhere shows evidence of necrosis.

Section 2. Shows a number of large homogeneous structureless pink-stained areas, scattered throughout which there is considerable nuclear fragments and dust. Surrounding these areas there is a zone of epithelioid cells, and nearby these larger areas there are a few small (about one-sixth low-power field size) areas showing numerous epithelioid cells, scattered giant cells and peripheral nuclei, and about these a zone of small mononuclear cells. Also, in the neighborhood of these areas, the lung tissue is greatly scarred; there is considerable coal pigment and scattered small to fair-sized hemorrhages. A great many of the alveoli and bronchioles in the neighborhood are collapsed and in the walls there are seen several scattered typical proliferative miliary tubercles.

Section 3. Shows great scarring of the lung tissue and the scared tissue has the appearance of hyalinization. There is considerable coal pigment scattered throughout. The alveoli and bronchioles are completely collapsed in great part. In places the scar formation is not so dense and here there are numerous prominent bloodvessels. In the section there is a portion of a large bronchus. At one place near the mucous glands there are seen three strips of true bone, composed of typical osteoblasts, surrounded by a homogeneous bluish-pink matrix, and surrounding these there is a thin layer of connective tissue. In the lumen of this bronchus there is a considerable amount of mucus, numerous polymorphonuclear leukocytes, a moderate number of mononuclear cells and

cell fragments. In places there is considerable desquamation of the epithelium. The connective tissue of the wall is increased in amount, in places very dense, homogenous, suggesting early hyalinization. In areas there are many dilated capillaries and scattered accumulations of round cells.

In all sections of the lung there are scattered areas in which the walls of groups of the alveoli are ruptured and good-sized spaces formed thereby. Some of these dilated spaces contain exudate similar to that described above.

Liver. Lobulation fairly distinct and fairly regular in the section. The cells all show evidence of postmortem change and are swollen and granular. They are slightly separated from each other. The cells in the central portion throughout contain much brown pigment. The capillaries contain many polymorphonuclear leukocytes.

Spleen. Shows a very slightly diffusely thickened capsule. The trabeculæ are moderately increased in size and number; the Malpighian bodies are small, in places consisting of but a few cells about a bloodvessel and trabeculum. The nucleated cells in the pulp, however, are greatly increased in number. Scattered throughout the spleen there is a moderate amount of intra- and extracellular brown pigment. With the high power the sinuses seem to contain in places many polymorphonuclear leukocytes.

Pancreas. The tissue shows evidence of moderate postmortem change. The islands of Langerhans are fairly numerous and of good size. They show an apparent change, except that about a number of them there is an increase in the reticulum of the pancreas. The remainder of the parenchyma shows no other abnormality except that noted above.

Adrenal. There is some thickening of the capsule; the glomerular zone is not as prominent as normal; the tissue throughout shows evidence of moderate postmortem change. In the medulla there is a circumscribed area equal to a few low-power fields in which there are many large cells lying close to one another, suggesting ganglion cells. Some of these contain more than one nucleus.

Thyroid. The acini in general are of average size, lined by flat to cuboidal epithelium. Filled with amorphous deeply pink-stained material. The stroma is increased moderately in amount. In the regions of the increase the acini show slight to considerable atrophy. In one portion of the section there are three small circumscribed areas, one of them composed of acini much like those of the gland. The other two composed of smaller acini lined by cuboidal epithelium, more like the thyroid tissue of a child. About these areas there is a thick connective-tissue capsule.

Case II.—The Son. J. G., aged seventeen years; undersized for his age; an errand boy. Mentally he is distinctly below normal. Has been in a reformatory for three years.

He has adenoid facies and both upper lids droop, the right more than the left. In looking from the horizontal plane the middle of the upper lid crosses the iris of the pupils. Two median incisor teeth of the upper jaw missing, some of the lower in bad order. Numerous glands, supraclavicular, discrete, the size of an almond. The same is true in the axilla. Inguinals normal in size. Epitrochlears normal.

The whole complexion is dark. In addition there are numerous freckles all over the neck and trunk as far as the groin of both legs; these are dark brown in color, about 2 mm. in size. In addition there are about twenty larger areas of pigmentation; these are oval in shape, circular and vary in size from 1 to 5 cm. in diameter; they are darker in color and not elevated. There are few fibromata, one over the right clavicle, one on each forearm, one on the left upper arm and three on the back. There is one chalazion on the left upper lid and two on the lower lids. No hair in the axillæ and the areola of nipples are dark, 3 cm. in diameter. Eyes are prominent. There is a fibroma on the left supra-orbital ridge and on the left upper part of the chin.

Lungs. Negative.

Heart. Upper border, third rib; right border, right border of sternum; left border, 8 cm. from midsternal line. Apex beat not visible but palpable in the fifth space, 9 cm. from the median line. Heart action regular; normal in rate; no murmurs. Radials equal; regular; no increased tension; some thickening (pseudosclerosis).

Liver, Spleen, Kidneys and Abdomen. Negative.

Knee-jerks. Active.

Extremities. No edema.

Genitalia. Negative except for absence of pubic hair.

Has three brothers and four sisters who are said to be normal, excepting the one mentioned above, who has Hirschsprung's disease.

SUMMARY. 1. A description has been given of the occurrence of von Recklinghausen's disease in a father and son, with the autopsy findings in the case of the father, in whom the disease lasted thirteen years.

2. The presence of the disease in the son, associated with definite mental inferiority and delayed sexual development.

3. A review and analysis of the literature of 243 cases of multiple neurofibromatosis.

4. An analysis of 30 cases of the familial type, with charts of families in which there were two or more affected persons in one family. This establishes its hereditary tendency, showing the hereditary factor to be dominant, there being something in the germ plasm that positively facilitates the production, under appropriate stimulation, of tumors of the nerve sheaths.

5. The relation of neurofibromatosis to malignancy.

In conclusion, we wish to express our thanks to Dr. S. Wachsmann, medical director of Montefiore Home and Hospital, for permission to publish this case; to Dr. B. S. Oppenheimer, attending physician to Montefiore Home and Hospital, for many valuable suggestions in the preparation of this paper; and to Dr. B. S. Klein, pathologist to Montefiore Home and Hospital, for the preparation of the microscopic sections.

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THE TEETH AND TONSILS AS CAUSATIVE FACTORS IN ARTHRITIS.

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From the earliest days of medical science the teeth and tonsils have been considered as having a causal relationship to arthritis. This is shown by the use of the terms "rheumatic tonsils" and "gouty gums." These conditions were formerly supposed to be induced by exposure to cold or to an excess of uric acid or lactic acid in the blood, or to some unknown disturbance of the metabolism.

Of late years the infectious theory of arthritis has been steadily gaining ground. This theory results from the discovery of microorganisms in or around the joints and also because arthritis has been observed frequently to follow various local and general infections.

The conception that a general systemic disease, such as arthritis, could arise from a local infection was appreciated early in the development of medical science. Until recent years, however, the apparent connection was recognized only when a condition of surgical sepsis preceded the arthritis.

The newer concept of the subject, to which the term focal infection has been applied, presupposes a circumscribed area of tissue infected with microörganisms. This area of infected tissue, the primary focus, is generally obscure in nature, often difficult to locate, and usually has no apparent connection with the secondary focus located in the articular structures. The broader interest in this subject has been brought about by a better knowledge of bacteriology, of modes of infection and by coöperative laboratory and clinical research.

Chronic infection of the tonsils and lymphoid tissue of the nasopharynx is exceedingly common in childhood, while acute rheumatic fever is relatively rare at that age. On the other hand the onset of rheumatic fever following an infection of the mouth and throat is too well recognized to be controverted.

Alveolar abscess is so prevalent as to be regarded as well-nigh universal, and yet it is not commonly associated with systemic infection. The protective forces surrounding the abscess are so efficient in the great majority of instances, and the lesion becomes so thoroughly walled off, that many thoughtful physicians and dentists deny the possibility of this condition becoming a focus of infection except on rare occasions.[1]

[1] Billings, Frank: Focal Infection, New York, 1916, 6.

In certain cases, however, the etiological relation of localized infection to both acute and chronic systemic disease seems too evident to be set aside. Numerous cases reported by various workers testify to the marked improvement observed when a localized area of infection has been removed.

The bacteria most commonly found in areas of local infection are the members of the streptococcus group. Their usual habitats are the regions of the teeth, the tonsils and the nasal accessory sinuses. Careful questioning will often elicit symptoms pointing to existing infection in these structures or in some other part of the body.

A coöperative study of the patient should be made, including examinations by dentists, by ear, nose and throat surgeons, and when necessary by other specialists. A careful roentgen-ray study of the teeth and accessory sinuses is always advisable and frequently absolutely indispensable.

Laboratory examinations of pathological material should always be made. Cultures should be taken from the depths of tonsillar pockets and alveolar abscesses and not from the surface of the gums or tonsils.

In addition, it is necessary to examine fluid aspirated from joints or small bits of synovial membrane or lymph glands, or muscle tissue may be removed for pathological study. A Wassermann test should always be made to eliminate a syphilitic joint involvement.

The work of Rosenow[2] has shown what is apparently a remarkable transmutability of the members of the streptococcus group. A strain of the Streptococcus viridans isolated from the blood of a case of chronic infectious endocarditis was cultivated in various media, and animals were inoculated with successive strains. The end-result was a pneumococcus. The bacteria were typical pneumococci and transmutation of the original pure culture of Streptococcus viridans had occurred in form, cultural characteristics and in general and special pathogenic virulence for animals. Rosenow has also observed that the property of transmutation is reversible within the members of this family.

Many eminent bacteriologists in this country have been unable to duplicate Rosenow's[3] experiments in bringing about transmutation of the members of the streptococcus group, and his conclusions are not accepted by many equally prominent laboratory workers.

The results of Rosenow's experiments show that the streptococci often have a remarkable affinity or tropism for the organs or tissues from which they were isolated.

At autopsy oftentimes no other focal lesions could be found

[2] Transmutations within the Streptococcus Pneumococcus Group, Jour. Infect. Dis., 1914, xiv, 1.

[3] Elective Localization of Streptococci, Jour. Am. Med. Assn., 1915, lxv, 1687.

except those in the organ in question. The cells of the tissues for which a given strain shows elective affinity take the bacteria out of the blood stream as if by a magnet.

Individual animals, like human beings, are found to vary in their ability to resist infection. Certain virulent bacteria seem to have the property of rendering the tissues less favorable for their growth. On the other hand the less virulent bacteria tend to make this soil more favorable. Some property evidently exists in the tissues of the individual harboring a focus of infection which permit the bacteria to develop changes in virulence under varying degrees of oxygen pressure and in mixed culture. The susceptibility of the host is far more important than the specificity of the infecting microörganism.

Diseased Conditions of the Teeth and Arthritis. Over a century ago Benjamin Rush[4] reported the cure of a case of rheumatism in the hip-joint by extracting a tooth. Referring to decayed teeth he says: "I am disposed to believe that they are often the unsuspected causes of general and particularly of nervous diseases. . . . Our success in the treatment of all chronic diseases would be very much promoted by directing our inquiries into the state of the teeth in sick people and by advising their extraction in every case in which they are decayed. It is not necessary that they should be attended with pain in order to produce diseases." In the light of modern scientific work the above statement is almost prophetic.

Apparently no further attention was paid to this subject until the latter part of the nineteenth century, when we find Ingersoll,[5] Witzel[6] and Reese[7] advocating the removal of all decayed teeth which are not absolutely necessary for good articulation. In 1899 William Hunter[8] called attention to diseased conditions in the teeth, gums and alveolar processes and suggested the term "oral sepsis" or medical sepsis. He believed it to be of much more common occurrence than surgical sepsis. His article included a scathing denunciation of American mechanical dentistry, with special reference to crown- and bridge-work and the stomatitis existing under artificial plates. With our present knowledge this criticism was more or less justified.

Shortly afterward Price[9] referred to root canals as the "dentists' graveyard, where so many cover up careless and defective work, trusting it will never come to light."

[4] Medical Inquiries and Observations, Philadelphia, 1819, i, 1917.

[5] Sanguinary Calculus, Ohio State Jour. Dent. Sc., 1899, i, 189.

[6] The Treatment of Pyorrhea Alveolaris or Infectious Alveolitis, British Jour. Dent. Sc., 1882, xxv, 153.

[7] Uremia and its Effects upon the Teeth, Dental Cosmos, 1886, xxviii, 550.

[8] Dental Diseases in Relation to General Diseases, Especially to Infective Gastritis, Odont. Soc. Tr., 1898–99, xxi, 92.

[9] Practical Progress in Dental Skiagraphy, Items of Interest, 1901, xxiii, 458.

Broomell[10] called attention to the deleterious effects of inserting large gold fillings near living tooth pulps and likewise the placing of gold-shell crowns without removing the pulp. Chayes[11] has characterized mechanical bridge-work as unsatisfactory, incomplete, unwholesome and unclean.

Kenneth Goadby[12] was the first to point out the direct relationship of dental infections to joint infections. By the removal of infected teeth he was able to produce a cure in 3 cases, one of which had been completely disabled for many months. From these patients he isolated an organism which he called the Streptobacillus malæ. This organism by animal inoculation produced joint disease in rabbits

Hartzell and Henrici[13] have for several years conducted a systematic research, including animal inoculation, into the relationship of mouth infection to metastatic infection of other parts of the body. Patients presenting joint infection were referred to them for investigation and treatment of mouth conditions. A complete roentgenographic examination of the teeth and jaws was first made. Whenever dental abscesses were present the abscessed teeth were isolated with dry gauze, the tooth or root was cleansed with iodin and wherever possible the tissue about the neck of the tooth was cauterized. The tooth was extracted and the root tip amputated with sterile forceps and immediately dropped into culture media. The resulting growth has invariably produced, among other bacteria, the Streptococcus viridans. This organism was found in the confined dental abscess, in the superficial tissues of the peridental membrane and even in the roots of healthy living teeth. These writers believe that the dental path is commonly infected with this organism.

Susceptibility of the Tooth to Infection. Certain anatomical conditions resulting from the development of the teeth render them particularly susceptible to infection from without. The union of the mucous membrane to the tooth structure is always imperfect and capable of admitting infection. The dental structure has no protecting device save its coat of enamel. If this be in any way imperfect there are no antibodies or protecting leukocytes in the saliva to save it from the disintegrating effect of bacterial action.

The structures about the tooth are not well adapted to resist infection from the tooth. The gingival crevice, or gum marginal crevice, is protected externally by tough pavement epithelium, but has almost no epithelial protection at its point of union with the tooth itself. Through destruction of enamel, dentin and from

[10] The Adventitious Effects of Large Masses of Gold in Contact with Tooth Tissues, Dental Cosmos, 1910, lii, 389.

[11] Empiricism of Bridge-work, Items of Interest, 1910, xxxii, 745.

[12] The Relation of Diseases of the Mouth to Rheumatism, Practitioner, 1912, lxxxviii, 107.

[13] The Dental Path: its Importance as an Avenue to Infection, Surg., Gynec. and Obst., 1916, xxii, 18.

suppurating pulps the teeth present 32 separate sources of infection. There are also 32 open dental alveoli and 30 spaces between the teeth which are susceptible to infection. The generous blood supply at this point allows microörganisms to pass readily into the openings in the bottom of this crevice and so into the deeper tissues by way of the lymph and blood streams.

Microörganisms have been found in freshly opened pulp chambers where no evidence of disease existed. A putrescent mass in the pulp chamber may exist for months or years because the walls cannot collapse and are incapable of bringing about the natural cure of an abscess as is possible in other parts of the body.

Pyorrhea Alveolaris. This disease has been recognized for several centuries, but was first described by Riggs in 1867. It is strictly a disease of the peridental membrane and is indicated by a progressive destruction of the root membrane of the tooth commencing at the gingival border, generally accompanied by a flow of pus and destruction of the alveolar walls. Pus is absorbed into the blood and lymph channels, into the tissues adjacent to the teeth and from the gastro-intestinal tract by swallowing. A few years ago a considerable furor was created in the profession by the discovery of the Endameba buccalis in the pyorrheal pockets of those suffering from the disease. This protozoa had been long known, but Barrett[14] was the first to consider it as an etiological factor in pyorrhea alveolaris. Bass and Johns[15] believe it to be the cause of this disease.

On the other hand, Sanford and New[16] hold that before Endameba buccalis can be regarded as the cause of pyorrhea alveolaris its pathogenicity must be demonstrated by animal experimentation. They also believe that before the alkaloids of ipecac can be accepted as the cure of this disease it must be established that they actually destroy the amebæ in the mouth.

Billings[17] believes that the endamebæ play an important part and permit infection with the pyogenic bacteria. The bacteria are the important factors in causing the general infection.

Roentgenography in Dental Conditions. The roentgen rays are of the greatest value in accurately diagnosing certain diseased conditions of the teeth which are considered to have an etiological relation to arthritis. Probably its greatest field of usefulness is in locating abscesses around the apices of non-vital teeth. Such infections may occur without pain and without clinical evidence of their presence. If their location is such that they can discharge

[14] The Protozoa of the Mouth in Relation to Pyorrhea Alveolaris, Dental Cosmos, 1914, lvi, 948.

[15] Pyorrhea Dentalis and Alveolaris; Specific Cause and Treatment, Jour. Am. Med. Assn., 1915, lxiv, 553.

[16] The Relation of Amebiasis to Pyorrhea Alveolaris, Surg., Gynec. and Obst., 1916, xxii, 27.

[17] Focal Infection, New York, 1916, 6.

their contents into the system—for example, by way of the antrum —their presence may remain unsuspected until diagnosed by the roentgen rays. In other teeth the abscess may protrude as the familiar gum-boil, which ruptures and may finally establish a fistula.

It must be clearly stated at the outset that an abscess may exist which cannot be revealed by the roentgen rays. This is because the pus is thinly distributed in a certain area or because the bone has not been sufficiently robbed of its lime salts to make this loss clear on the roentgenogram. The first appearance is a small area of slight bone rarefaction around the root apex. This process may go on to destruction of bone with cavity formation, resulting in the blind dental abscess or a fistulous connection with the mouth may be established. These blind abscesses often heal spontaneously. Under such favorable conditions the laying down of lime salts and the subsequent regeneration of bone can be followed with precision in roentgenograms made at intervals.

The interpretation of dental roentgenograms is full of pitfalls. Unless one is familiar with dental anatomy and pathology, and the varying appearance of shadows produced by roentgenograms taken from different angles, serious errors will be made. It is possible to take a roentgenogram from such an angle that an apical abscess is apparently demonstrated. A plate or film made from a slightly different angle will disclose only the normal bone surrounding the tooth apex. The reason for this error lies in the fact that at certain angles the shadows of the nasal cavity or antrum may overlie the tooth root and simulate the appearance of an abscess.

The point is that an apical shadow merely signifies decalcification of bone from any cause. It may represent a slow change, such as atrophy or absorption from long-continued irritation or pressure; it may mean an acute infective process or it may signify the remains of former disease—scar tissue. These shadows do not necessarily indicate the presence or absence of pus. This fact can be determined only by a study and correlation of the symptoms and clinical findings.

Other conditions which may cause symptoms referable to the teeth, and which can be differentiated by the roentgen rays, are calcareous concretions or stones in the pulp of the teeth, cysts of the jaw, dentigerous cysts and unerupted or impacted teeth.

Relation of Dental Infection to Systemic Conditions. In many cases there is a tendency to overestimate the role of these infections in causing more serious diseases. It is difficult to establish the etiology, as, for example, in a case of chronic arthritis of several years' standing. Dental examination shows several non-vital teeth. The roentgenogram may reveal any degree of change from a slight rarefaction of bone to a blind abscess. The teeth have been filled for many years and have given no trouble. The joint infection is hematogenous and a certain percentage of periapical

infections are hematogenous. Why may not both of these infections have resulted from a mild general bacteriemia and have developed coincidentally? Also, if the joint condition came first, why may it not have caused the dental condition? Other infections are quite as likely the cause as those in the mouth. Arthritic cases by no means always clear up after mouth infection has been removed. Many innocent teeth are being sacrificed from insufficient data, such as a crudely interpreted roentgenogram. Worse than this, several fatalities from ill-advised extraction of teeth during periods of exacerbation have been reported. It is well to remember the remarkable ability of the tooth and adjacent structures to bring about the spontaneous cure of a blind dental abscess with no resulting systemic involvement. Were this not so the human race would long since have been exterminated.

Diseased Tonsils and Arthritis. The close connection between tonsillitis and arthritis has been recognized for at least a century and probably much longer. At times the joint and throat symptoms are simultaneous in their onset; at other times the tonsillitis precedes the arthritis and may even completely subside before the joint lesions develop. Subacute and chronic infectious arthritis are often associated with recurring attacks of tonsillitis, the tonsils lighting up previous to each fresh exacerbation of the joint lesions. On the other hand the tonsils may be the seat of a low-grade chronic inflammation lasting for months, with frequent outbreaks of a more acute character.

The pathological conditions to which the tonsils are subject are generally attributed to the peculiar anatomical structure of the crypts and their tendency to retain cellular débris. The crypts are tortuous and deep, extending nearly to the capsule; their walls are held in close apposition by pressure of the surrounding lymphoid tissue. The mouths of the crypts may be partially closed by the plica triangularis or the upper wall of the supratonsillar fossa, and, in addition, the supratonsillar crypts drain upward. The result is that a certain amount of débris is found in the crypts of all tonsils. Bacteria enter the crypts and develop under ideal conditions for growth. The cryptic epithelium is usually composed of only one or two layers of cells and offers little mechanical resistance to the entrance of foreign material. The conditions are thus seen to be ideal for the invasion of bacteria and the absorption of the toxic products of their growth.

Disease in the middle ear, the accessory sinuses, conjunctivæ, teeth and alveolar processes may be the cause of chronic disease of the tonsils. On the other hand, obstruction of the upper air passages by hypertrophy of the tonsils and adenoid overgrowth prevents proper drainage from the nasal cavities and accessory sinuses and leads to infection of the middle ear, the sinuses of the head and the mucous membrane covering the turbinate bodies.

In subacute and chronic arthritis the deep crypts almost invariably show pure cultures of the Streptococcus hemolyticus, which produce acute or chronic multiple arthritis when injected into animals

The presence of these organisms in the tonsillar crypts of patients with joint lesions and the experimental results in animals suggest a causal relationship of the tonsils to arthritis.

Operations on the Tonsils. The advocates of partial removal have been influenced by the possible loss of some unknown function which would be detrimental to the patient and have counselled against complete removal of the tonsils. Those who believe in the operation of complete tonsillectomy point out the fact that thousands of these operations have been performed of late years, with no untoward result which could be attributed to the loss of any possible functionating power. It is also said that the histological structure of the tonsils shows that their function, whatever it may be, is identical with that of other lymphoid nodules of the body. This function, they claim, would no more be missed than the removal of a small piece of skin.

In the absence of any definite theory as to their function it seems reasonable to believe that they have a purpose even if it has not so far been discovered. They should never be removed, especially in children, without adequate cause. Before advising ablation the physician should be convinced that the tonsil is so completely diseased that it cannot functionate properly. Many tonsils are capable of overcoming infection in certain of their crypts. As a result a healed process may be present which, to the inexperienced, would denote active disease.

Wright[18] and others assert that the tonsils enlarge regularly during the periods of dentition, the enlargements occurring about the second, sixth, twelfth and seventeenth years. These enlarged tonsils, if not infected, return to normal when the teeth have completely erupted. This is a most potent argument against their removal at these periods, when the hypertrophy is evidently a response to some physiological stimulus.

Crowe, Watkins and Rothholz[19] believe that partial occlusion of the crypts from partial tonsillectomy renders the patient more liable to secondary cardiac, joint and renal lesions. They have observed 8 cases with frequent attacks of tonsillitis for many years preceding, but never with anything but local symptoms. With the idea of stopping these attacks each of these patients had had a partial tonsillectomy performed with the guillotine or with the electric cautery under local anesthesia in each case. All went well

[18] A Functional Relation of the Tonsil to the Teeth, Boston Med. and Surg. Jour., 1909, clx, 635.

[19] Relation of Tonsillar and Nasopharyngeal Infections to General Systemic Disorders, Bull. Johns Hopkins Hosp., 1917, xxviii, 1.

until the next coryza, when joint symptoms appeared for the first time. Portions of the tonsils showed the crypts obscured by scar tissue. After their removal the joint symptoms gradually disappeared and the temperature returned to normal. The partial tonsillectomy, by narrowing the orifices of the crypts of the remaining portion of the tonsil, favored the retention of bacteria and pathological detritus and made the conditions more favorable for a general infection.

The end-results of 1000 tonsillectomies performed during the past five years at the Johns Hopkins Hospital have been carefully studied. These operations were performed under the rigorous routine of a surgical ward, with experienced anesthetists and assistants, and were regarded as major surgical operations. The cases were followed up in order to learn the subsequent history of disorders supposed to be secondary to a chronic focus of infection in the upper air passages.

In the "arthritis group" four classes of cases are recognized: (1) infectious arthritis; (2) myalgia; (3) rheumatoid arthritis; (4) acute rheumatic fever.

1. *Infectious Arthritis.* Tonsils and adenoids were removed in 91 cases. The ultimate result was noted in 31. In 24 the joints are normal; 4 are improved although the joints have never entirely cleared up; 2 are not improved; 1 is worse than at the time of operation.

2. *Myalgia.* Four cases were followed up after tonsillectomy. All are well.

3. *Rheumatoid Arthritis.* Nine cases were followed up. Only 2 are improved; 2 are not improved, but no new joints are involved; 5 cases are much worse.

The conclusion drawn from this group of cases is that only in very exceptional circumstances should one subject a patient with rheumatoid arthritis to an operation for the removal of tonsils. These patients are for the most part middle-aged people. Their disease is well advanced when they seek medical advice. There is often marked anemia and a distinct lessening of their ability to withstand pain. After such a trying operation as tonsillectomy it often requires many weeks or months before the patient regains the physical condition present at the time the tonsillectomy was performed.

4. *Acute Rheumatic Fever.* Twenty-five cases were followed up; 4 of these cases had a recurrence, 1 of which had been perfectly well after the removal of his tonsils.

It is quite evident that the tonsils are not the only portal of entry for the organisms that cause rheumatic fever.

Opinions of Orthopedic Surgeons. With a view to ascertaining the opinion of medical men who have an exceptional opportunity of studying cases of arthritis a series of questions was submitted to 177 orthopedic surgeons throughout the country.

The questions called for answers with definite figures and not for opinions or beliefs.

The replies show the trend of present medical thought. They also show that a large percentage of orthopedic surgeons replying to the questionnaire believe that the removal of so-called foci of infections in teeth and tonsils have produced improvement and cure in many cases of acute and chronic arthritis. The beneficial results are more evident in acute than in chronic arthritis. If removal of foci in the teeth and tonsils does not bring about improvement the majority of these surgeons depend upon general hygienic or stimulative treatment. A small percentage continue the search for other foci, with special reference to the gastro-intestinal tract. It is interesting to note that opinion as to the accuracy of the statement that most foci of infection are to be found in the head is equally divided.

Statistics of the Writer's Cases. For several years the writer has conducted an investigation of the relation of diseased conditions of the teeth and tonsils to arthritis. The study was made in collaboration with dentists and ear, nose and throat surgeons, and included both hospital and private patients.

It was determined at the outset to leave the diagnosis and treatment of dental and tonsillar conditions entirely to the judgment of these specialists and to abide by their decision in each case. The results were determined by the patients' statements and by examination as to general health and condition of the joints. It was attempted to ascertain if operations on the teeth and tonsils had produced in the joints:

1. Cure.
2. Relief of symptoms.
3. No improvement.
4. Aggravation of symptoms.

Whenever possible the patients were referred back to the special surgeon for reëxamination and after treatment following any operative procedure.

It is often impossible to determine what element in the treatment is responsible for the improvement or cure. Appropriate treatment for arthritis was instituted at the time the mouth and throat condition was being investigated and treated. When improvement is no more rapid than has been noticed for years under approved treatment for arthritis it is natural to attribute the progress to the true and tried methods.

Total number of cases, 40.

1. Diseased conditions of the teeth and tonsils, 29 cases: Of these (*a*) 12 were of the teeth alone; (*b*) 11 were of the tonsils alone; (*c*) 6 were of both teeth and tonsils.

2. Negative dental and nose and throat conditions, 8 cases: Of these 3 improved under treatment for arthritis; 2 were unimproved under treatment for arthritis; 3 could not be traced.

3. Dental and nose and throat examinations were not made in 3 cases: Of these 1 improved under treatment for arthritis; 2 could not be traced.

1 (*a*) Diseased conditions of the teeth alone, 12 cases: Of these 3 showed some improvement in the arthritis; 1 showed striking and immediate improvement; 3 improved after an interval of time had elapsed (1 of these last after several doses of autogenous vaccine); 2 were unimproved, all after the extraction of teeth; 1 was unimproved after a pyorrhea had been treated; 1 improved without operation; 1 could not be traced.

1 (*b*) Diseased conditions of the tonsils alone, 11 cases: Of these 2 were improved after tonsillectomy (1 of these was cured); 1 was unimproved after tonsillectomy; 1 was unimproved without tonsillectomy; 1 began to improve before tonsillectomy was performed; 1 was worse after tonsillectomy; 1 had a relapse after a tonsillectomy performed one year before; 1 refused operation.

1 (*c*) Diseased conditions of both teeth and tonsils, 6 cases: Of these 1 improved after extraction of teeth but relapsed later; 1 improved without operation; 1 was unimproved after extraction of teeth; 1 was unimproved after extraction of teeth and tonsillectomy; 1 was unimproved where operations were not performed; 1 refused operation.

In analyzing the above cases it will be seen that there was but one case which showed immediate improvement, which could be classed as a cure, following extraction of teeth, and but one such result following tonsillectomy.

Many of these cases which are classed as improved showed the improvement in their general health rather than in a changed appearance of the joints. It has seemed fair to consider them as better even if the improvement were slight.

In these few cases the improvement following proper treatment of dental disease was more noticeable than the improvement following operations on diseased tonsils.

In speaking of the above cases as improved or unimproved, either with or without operations on the teeth or tonsils, it is not implied that the operation, or the lack of operation, is responsible for the present condition of the patient. Many factors influence the result, and it is intended merely to state the condition of the patient when last seen.

As has been noted by others, diseased conditions of the teeth have been found more often in adults and diseased conditions of the tonsils more often in childhood.

SUMMARY. The relation of the teeth and tonsils to arthritis is at present a moot question. Billings and his followers point to the careful work of Rosenow and others on the bacteriology of arthritis and to the numerous cases of improvement and cure of arthritis following removal of diseased teeth and tonsils. They believe that

this proves the accuracy of their contention that a focus of infection exists in the head in many of these cases. On the other hand, many trained pathologists and reputable clinicians have been unable to reproduce either the laboratory findings or the clinical results of the Chicago workers. Consequently they either reject the theory as a whole or accept it in a greatly modified form. It is probable that the pendulum has swung too far in the direction of the wholesale removal of teeth and tonsils. The truth will probably be found in a middle ground somewhere between these divergent theories.

There is undoubted improvement in numerous cases of arthritis following the removal of an abscessed tooth or a diseased tonsil or when a case of active pyorrhea has received proper treatment. On the contrary, many such cases are given similar careful treatment without affecting the progress of the joint condition in the slightest degree.

One reason for the failure to obtain successful results in arthritis by treatment of dental and tonsillar disease is that the cases have been selected without knowledge of the exact pathological condition present in the organ in question. Many apical abscesses in which nature had effected a cure by walling off the disease have been treated by extraction of teeth. This has resulted not only in the loss of valuable teeth, but has at times been the cause of a dissemination of the infection to other parts of the body, with dire results.

In the same way the crypts in certain areas of a tonsil may overcome an existing infection. These crypts are perfectly harmless. A tonsil in which the crypts are seared over by scar tissue, perhaps as the result of an incomplete tonsillectomy, may be a source of potent danger if the crypts contain an active focus of infection.

Success in treatment of these foci lies with the men who can distinguish the apical abscess and the diseased tonsil which are overcoming their infection by nature's methods. They must know by careful and special training when a tooth or a tonsil are active agents of infection. Such knowledge must be supplemented by accurate interpretation of dental roentgenograms and skilful laboratory work. Trite as the saying is, coöperation in such endeavor is the keynote of success.

Another reason for failure to alleviate arthritic cases is due to the fact that the focus of infection lies in some other part of the body. It may be discovered by further careful search in the lungs, heart, kidneys, genito-urinary or gastro-intestinal tracts, ductless glands, the nervous system and elsewhere. A certain number of cases are due to syphilis and to tuberculosis. Unfortunately in many cases it is never brought to light.

Many cases of arthritis are believed by thoughtful physicians to be due not to a localized collection of microörganisms but to an entirely different etiology. This class of cases is supposed to result from some disturbance of the metabolism, probably chemical in nature, which produces joint changes not always to be distinguished

from those caused by bacterial agency. They compose a fairly large share of the cases of chronic progressive arthritis seen in the daily routine of practice. A general flaccidity of tissues and relaxation of important organs accompanied by ptosis of the abdominal viscera often characterize these cases.

In acute arthritis the probability of producing a cure or improvement by the removal of a supposed focus in the teeth or tonsils is greater than in cases in the chronic stage. It is unreasonable to suppose that a restoration of function can be brought about in joints where extensive pathological changes have taken place.

One very suggestive fact brought out in this investigation has been the marked improvement in the general health of the patients when diseased conditions of the teeth and tonsils have been properly treated. It oftentimes seems as if a millstone had been removed from their necks. This is noted very commonly even when no change was apparent in the joint condition.

EXPERIMENTAL LESIONS IN THE CERVICAL SYMPATHETIC GANGLIA IN RELATION TO EXOPHTHALMIC GOITER.[1]

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That exophthalmic goiter, the clinical manifestations of which are due essentially to a greatly increased protein metabolism, is the joint result of disturbance in the several glands concerned with metabolism there can be little doubt. The fact that the thyroid shows a pronounced and constant series of functional changes parallel with the course of the disease and the further fact that removal of the gland arrests the symptoms is convincing though not absolute proof that the thyroid is the secretory gland the hyperfunction of which initiates the metabolic disturbance.

But is the primary hyperfunction of the thyroid the result of primary pathological change within the gland itself or of direct stimulation from its nerve supply? Cannon's[2] experimental production in cats of some of the symptoms of exophthalmic goiter by continuous stimulation of the thyroid through the sympathetic system suggests the latter. Durante and I[3] have shown that in all

[1] Presented before the Association of American Physicians, Atlantic City, N. J., May 3, 1917.

[2] Cannon, W. B., Binger, C. A. L., and Fitz, R.: Experimental Hyperthyroidism, Am. Jour. Physiol., 1914–15, xxxvi, 363–364.

[3] Wilson, L. B., and Durante, L.: Changes in the Superior Cervical Sympathetic Ganglia Removed for the Relief of Exophthalmos, Jour. Med. Research, 1916, N. S., xxxiv, 273–296. Wilson, L. B.: The Pathological Changes in the Sympathetic System in Goiter, Am. Jour. Med. Sc., 1916, cliii, 799–812. Wilson, L. B.: Further Study of the Histopathology of the Autonomic Nervous System in Goiter, Jour. Lab. and Clin. Med., 1917, ii, 295–307.

cases of exophthalmic goiter we have had an opportunity to examine there is a pronounced and constant pathological lesion in the cervical sympathetic ganglia from which the thyroid receives its entire nerve supply. There is much suggestive evidence that these pathological changes in the cervical sympathetic ganglia are the result of direct bacterial infection within the ganglia.

The object of the present series of experiments has been to determine the effect directly upon the cervical sympathetic ganglia and indirectly upon the thyroid of various forms of stimulation applied to the ganglia themselves in healthy animals. Goats have been used for the experiments almost exclusively, and the results on these animals only will be described herein. The goat is a very desirable animal for experiments on the sympathetic ganglia and the thyroid, since the tissue elements of both these organs in their normal and pathological morphology and their staining reactions closely resemble those of the tissue elements of the same organs in man.

Stimulation in some of the experiments has been produced by electricity; in most instances, however, the stimulus has been obtained by direct bacterial inoculation into the ganglia. Observations have been completed on nineteen goats, and are still in progress on six others.

Technic. *Electric Stimulation.* After proper etherization of a goat its right superior cervical sympathetic ganglion was exposed. The ganglion was then directly stimulated by a moderate tetanizing current for one second, at intervals of three seconds, for a period of one hour. During the experiment the animal's blood-pressure was taken and the amount of saliva excreted noted. After one hour the right cervical ganglion and the right lobe of the thyroid were removed with as little loss of blood as possible. The left superior cervical sympathetic ganglion was then exposed and stimulated in the same manner as the right had been, but for a period of five and a half hours. At the end of five and a half hours the left superior cervical sympathetic ganglion and the left lobe of the thyroid were removed. After removal the ganglia and the lobes of the thyroids were properly fixed and stained by various methods, the ganglia usually by Nissl's and Ramon y Cajal's methods and the thyroid with hematoxylin-eosin and by Bensley's acid-fuchsin-methylene-green after acetic-osmic-bichromate fixation.

Bacterial Stimulation. After properly etherizing a goat its right or left superior cervical sympathetic ganglion was exposed and a small quantity of a culture of some bacterium was injected into the capsule of the ganglion. The wound was closed with aseptic precautions and the goat placed under observation. The period of observation varied from three days to three months. A few of the animals died and in such instances complete postmortems were made. In some of the others the cervical sympathetic ganglia and the lobes of the thyroid from both sides were removed at oper-

ations. In the remainder of the goats only the injected ganglion and the thyroid lobe on the same side were removed and examined.

SUMMARY OF OBSERVATIONS. 1. The normal nerve cells of the cervical sympathetic ganglia in the adult goat closely resemble the normal nerve cells of the cervical sympathetic ganglia of the human adult, except that a relatively large number of them are binucleate. Similarly, the thyroid of the adult goat when at rest histologically closely resembles the resting adult human thyroid.

2. (*a*) Moderate electrical stimulation applied for one second at intervals of three seconds for a period of one hour to the superior cervical sympathetic ganglion of an adult goat appears to produce no marked changes in the blood-pressure or respiration. If there were any definite changes they were masked by the diffuse stimulation involving the vagus. There was marked salivation.

(*b*) Microscopically, after the electrical stimulation noted above a large number of the nerve cells of the stimulated ganglion were swollen and showed hyperchromatization. The demonstration of dissolution of the chromatin by Nissl's method or of the presence of lipoid changes by Sudan III and Ramon y Cajal's methods has not been possible in any of the cells.

(*c*) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen, their protoplasm distinctly granular and their nuclei well rounded. The acini were distended with a feebly staining secretion, the numerous large vacuoles in stained preparations of which indicated the liquid character of the secretion. The condition of the cells and colloid secretion was parallel in all respects to that found in the thyroids of early cases of exophthalmic goiter in the human subject.

3. (*a*) Moderate electrical stimulation applied to the superior cervical sympathetic ganglion for one second, at intervals of three seconds, throughout a period of five and a half hours, produced clinical changes similar to those noted in Paragraph 2.

(*b*) Microscopically, after the electrical stimulation noted above, many of the nerve cells were markedly swollen and showed intense hyperchromatization. Many were swollen, hydropic and with disseminated chromatin. Sudan III preparations, even when thoroughly differentiated, showed conclusive evidence of lipoid change. This was demonstrated by Ramon y Cajal's method.

(*c*) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen but not nearly so much so as in those thyroids in which stimulation had been applied for only one hour. The protoplasm was clear and the nuclei showed a tendency to crenation. The acini were usually more distended and were filled with colloid material, which was more densely stained and contained fewer vacuoles than that noted in Paragraph 2 (*b*). These changes were evidently the result of beginning exhaustion of the cells and resembled the changes in the thyroid in cases of exophthal-

mic goiter in the human subject in which remission of symptoms has already begun.

4. (*a*) After the injection of a virulent culture of Streptococcus hemolyticus into the capsule of the superior cervical sympathetic ganglion of goats the animals died within three days after exhibiting symptoms of an intense toxemia.

(*b*) Within the injected ganglion of such a goat the nerve cells were found to lie in greatly distended pericellular lymph spaces. They were markedly hyperchromatic and hydropic, with diffuse dissemination of the chromatin, or were more or less completely disintegrated. No evidence of lipoid change was demonstrated by the Sudan III or silver-impregnation methods.

(*c*) After the above injection the cells of the thyroid parenchyma were palely staining, not swollen and apparently not overfunctioning. The amount and character of the colloid within the acini was not distinguishable from normal.

5. After the injection of certain strains of Bacillus influenzæ of apparently low virulence no systemic reaction or histological lesions were demonstrated. After the injection of other strains more recently isolated a marked inflammatory reaction was found around the injected ganglia, though the goats had shown no symptoms. Changes within the ganglia and within the thyroid were indistinguishable from those within the ganglia and thyroids from the goats described in Paragraph 6.

6. (*a*) The injection of freshly isolated virulent cultures of Bacillus bronchisepticus into the superior cervical sympathetic ganglion of adult goats usually produced marked constitutional symptoms such as trembling, increase of temperature, and loss of appetite, and frequently caused death in from three days to three weeks. No exophthalmos was noted.

(*b*) Within the injected ganglion of such a goat many of the nerve cells in animals dying early were found to be markedly hyperchromatic; others were hydropic, with disseminated or invisible chromatin and more or less distorted nuclei within such cells. Sudan III and silver-impregnation preparations showed the presence of changed lipoids. In the ganglia of goats that lived three weeks or more there was unmistakable evidence of complete cell destruction, in some instances extending from the point of inoculation well into the ganglion. Lipoid pigmentation was distinctly shown by Sudan III and silver impregnation. Histologically, these changes were parallel to those found in the ganglia in cases of exophthalmic goitre in the human subject.

(*c*) In goats from which the thyroid had been removed in from three days to three weeks after the injection the cells of the thyroid parenchyma were actively functionating, as was evidenced by their swollen size, granular protoplasm, well-rounded nuclei and the presence of large quantities of feebly staining secretion within the

acini. The histological appearance was closely parallel with that found in the thyroid in early cases of exophthalmic goiter. When a period of three months had elapsed between inoculation and removal of the thyroid the thyroid parenchyma showed evidence of exhausted function in that the cells were no longer swollen, their nuclei were more or less crenated and the colloid secretion within the acini was densely staining.

CONCLUSION. From the above experiments it would appear that irritation from the presence of certain bacteria within the cervical sympathetic ganglia of the goat may produce histological pictures within the ganglia and in the thyroid which parallel those found in the various stages of progressive and regressive exophthalmic goiter. This evidence supports the suggestion that in exophthalmic goiter the thyroid receives its stimulus to overfunction through its nerve supply and as a result usually of a local infection in the cervical sympathetic ganglia.

A STATISTICAL STUDY OF THE RELATIONSHIP OF THE ORIGIN OF ECTOPIC CONTRACTIONS TO VENTRICULAR PREPONDERANCE AS SHOWN BY THE ELECTROCARDIOGRAPH.[1]

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THAT the form of the electrocardiogram may indicate relative ventricular preponderance has been known for some time, but the relationship of such preponderance to the origin of ectopic contractions has, so far as we are aware, never been made a subject of study. Is it not possible that there may be some underlying relationship between preponderance and ectopic contractions that has escaped our attention up to the present?

It was with this possibility in mind that we began the review of the 375 cases studied by means of the electrocardiograph within the past eighteen months. The study was made in the cardiographic laboratory of the University of Pittsburgh, School of Medicine, at St. Francis Hospital. Most of the electrocardiograms were taken on patients who presented some cardiac disturbance, although a few were taken on patients in whom no cardiac lesion was suspected.

In the determination of preponderance we have used the criteria of Lewis,[2] slightly modified. Lewis, following the teachings of

[1] R. B. Mellon Fellow in Internal Medicine, University of Pittsburgh, School of Medicine, Pittsburgh, Pa.

[2] Clinical Electrocardiography, Shaw & Sons, London, 1913. Observations upon Ventricular Hypertrophy, with Special Reference to Preponderance of One or Other Chamber, Heart, 1914, No. 4, v, 367–402.

Einthoven,[3] believes that those curves which show the deepest deflection in lead I and the tallest summit in lead III indicate a relative preponderance of the right ventricle. The reverse of this picture—namely, the tallest summit in lead I and the deepest in lead III—is taken by him as indicative of preponderance of the

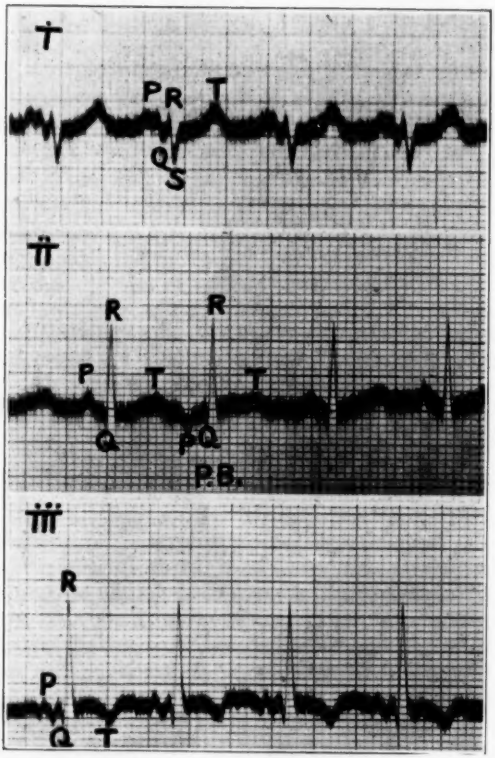

FIG. 1 (No. 289–2, leads I, II, III).—Electrocardiogram illustrating right ventricular preponderance. The *S* wave is deepest in lead I and the *R* wave is highest in lead III. This figure also illustrates a typical auricular premature contraction, in which the *P* is invert and the ventricular complex unchanged. There is no compensatory pause following the premature beat.

left ventricle, in which case there is a prominent *R* in the first lead accompanied by a diminutive *R* and exaggerated *S* in lead III. The modification used consisted merely in the inclusion in our statistics of those cases in which either *R* II or *S* II were greater than the corresponding waves in leads I or III, but in which consider-

[3] Arch. Internat. de Physiol., 1906, iv, 132; Arch. f. d. ges. Physiol., 1908, cxxii, 517 (quoted by Lewis).

ing leads I and III only there was a marked convergence of the *R* and *S* waves in cases of right ventricular preponderance and a marked divergence in cases of left ventricular preponderance.

Of the 375 cases studied, 136, or 36.2 per cent., showed left ventricular preponderance; 37 cases, or 9.8 per cent., showed right ventricular preponderance; while 202 cases, or 53.7 per cent.,

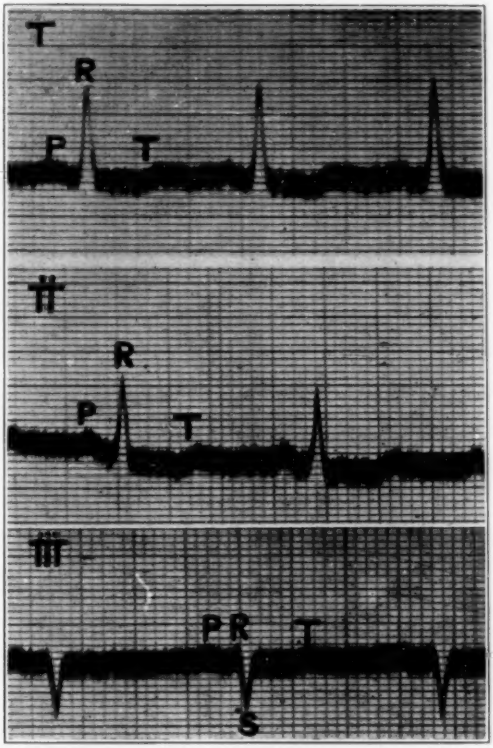

FIG. 2 (No. 359–1, leads I, II, III).—Electrocardiogram illustrating left ventricular preponderance. The *R* wave is highest in lead I and the *S* wave is deepest in lead III.

showed no relative preponderance. An apparent change in preponderance was noted in 8 cases, or 2.1 per cent., of which 2 showed a transition from left to right, or *vice versa*, 1 from right preponderance to no preponderance, or *vice versa*, and 5 from left preponderance to no preponderance, or *vice versa*.[4] Two other cases showed a doubtful

[4] Some of these changes may have been due to change of position of the patient, as often many e'grams were made on the same case and no separate record was kept of those e'grams taken in the upright and reclining postures.

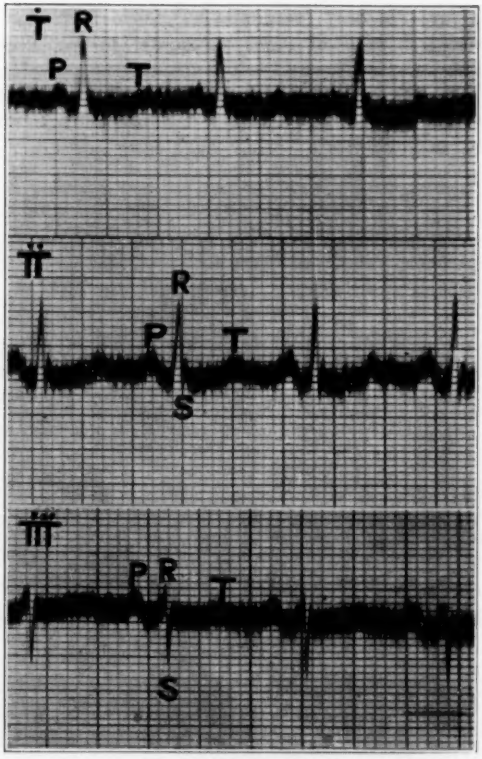

FIG. 3 (212–1, leads I, II, III).—Electrocardiogram not strictly fulfilling Lewis's criteria but representative of the type of case included in our modification as showing left ventricular preponderance. Note the *R* wave of lead II is higher than that of lead I, but the divergence of the *R* and *S* waves of leads I and III respectively is marked.

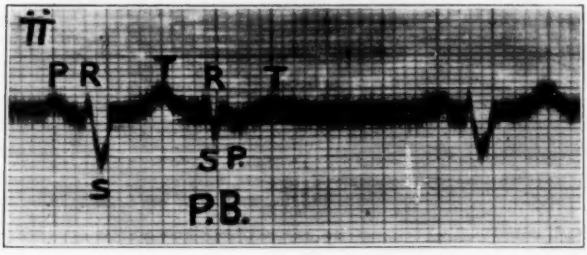

FIG. 4 (No. 210–10*a*, lead II).—Electrocardiogram illustrating a premature contraction arising in the auriculoventricular tissues. A low origin in the junctional tissues is indicated by the *R–P* sequence.

transition, but, as in the case of all figures in this paper, these doubtful cases were not included in the compilation of the statistics.

The relationship of the origin of ectopic beats[5] to ventricular preponderance forms the main theme of this study. The three types of ectopic contractions are: (1) auricular, (2) junctional and (3) ventricular. The latter may be further subdivided into those

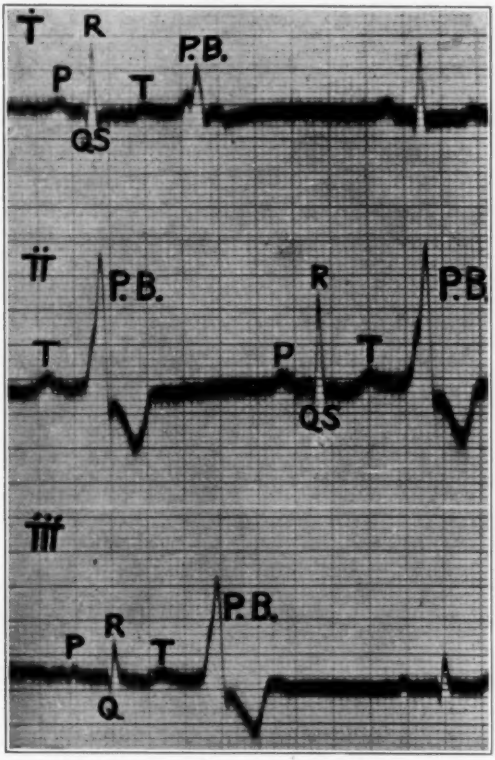

FIG. 5 (No. 149–14, leads I, II, III).—Electrocardiogram illustrating premature contractions arising in the right ventricle. The electrocardiogram also shows an absence of relative ventricular preponderance.

arising in the apical or left ventricular region and those arising near the base or right ventricle. We are not able at the present time to determine whether the ectopic beats arising in the auricle come from the left or right side, and although we know the relative position of beats arising in the atrioventricular tissue, that differentiation will

[5] We use the terms ectopic and premature and contractions and beats interchangeably in this paper.

not be considered in this communication. The characteristics of the several types of premature contractions need not be repeated here, as they are thoroughly familiar to everyone acquainted with the subject of electrocardiography and others will find a simple account in Lewis's book on *Clinical Electrocardiography*. The determination of the origin of ectopic beats is usually very simple, the

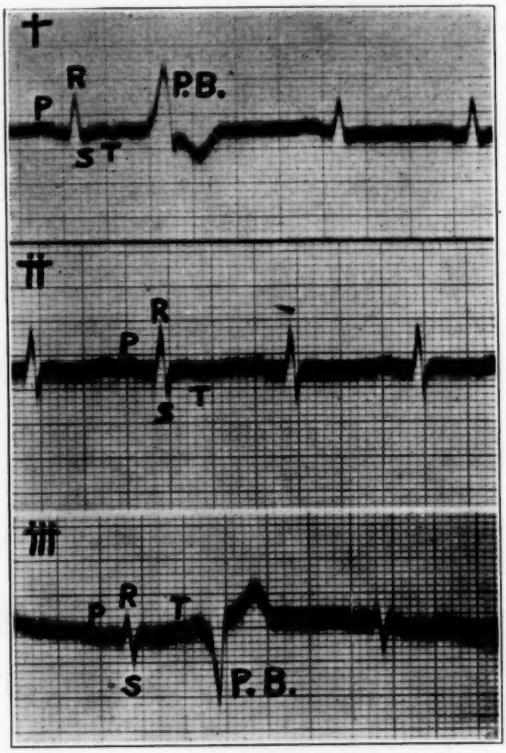

FIG. 6 (No. 130-1, leads I, II, III).—Electrocardiogram illustrating permature contractions arising in the left ventricle The premature beats are shown in leads I and III only.

single difficulty often encountered being in the differentiation of ventricular beats of right and left origin when occurring only in lead 1. In but 2 instances in our series did such premature contractions occur only in lead I, and these 2 cases were of the typical form of those of left ventricular origin, and are therefore included in the study.

Premature contractions (P. B.'s) of one type or another occurred 76 times (20.2 per cent.) in the 375 cases studied. Although it is

generally stated that an individual case usually shows but one type of premature beat, we found in our series 11 cases, or 17.4 per cent., which showed two different types, of which cases 2, or 3.2 per cent., showed ectopic beats arising in three different foci. Subtracting those cases counted twice or thrice we found ectopic beats in 63 different cases, or 16.8 per cent. of the series.

TABLE I.

		Per cent.
Cases showing left ventricular preponderance	136	36.5
" right ventricular preponderance	37	9.8
" no ventricular preponderance	202	53.7
Total number of cases in series	375	100.0
Cases showing left ventricular P. B.'s	30	8.0
" right ventricular P. B.'s	25	6.6
" auricular P. B.'s	11	2.9
" junctional P. B.'s	10	2.6
Total all cases of P. B.'s	76	20.1

A glance at Table I will show that premature beats arising in the left ventricle are the most common, with right ventricular premature beats running a close second. Next in order of frequency come auricular and junctional premature contractions which, in our series, occur in almost equal number. Ectopic beats of ventricular origin arising in both apical and basilar regions together are about five times more frequent than either auricular or atrioventricular premature contractions.

Can we analyze these cases further? Is there a causative relationship between preponderance and origin of ectopic beats? In an attempt to answer that question we present the following summary:

4 cases or 2.9 per cent. of left ventricular preponderance show auricular P. B.'s
1 case or 2.7 per cent. of right ventricular preponderance show auricular P. B.'s
6 cases or 3.0 per cent. of no preponderance show auricular P. B.'s

Total 11 cases or 2.9 per cent. of all cases show auricular P. B.'s

7 cases or 5.1 per cent. of left ventricular preponderance show junctional P. B.'s
0 cases or 0.0 per cent. of right ventricular preponderance show junctional P. B.'s
3 cases or 1.5 per cent. of no preponderance show junctional P. B.'s

Total 10 cases or 2.6 per cent. of all cases show junctional P. B.'s

13 cases or 9.5 per cent. of left ventricular preponderance show right ventricular P. B.'s
4 cases or 10.8 per cent. of right ventricular preponderance show right ventricular P. B.'s
8 cases or 3.9 per cent. of no preponderance show right ventricular P. B.'s

Total 25 cases or 6.6 per cent. of all cases show right ventricular P. B.'s

18 cases or 13.2 per cent. of left ventricular preponderance show left ventricular P. B.'s
1 case or 2.7 per cent. of right ventricular preponderance show left ventricular P. B.'s
11 cases or 5.4 per cent. of no preponderance show left ventricular P. B.'s

Total 30 cases or 8.0 per cent. of all cases show left ventricular P. B.'s

But brief comment is necessary, as the summary tells its own story. Auricular premature contractions occur in practically equal proportion in all types of preponderance. A greater percentage of left ventricular preponderance show junctional premature beats. Right ventricular premature beats occur in the largest percentage

in cases showing right ventricular preponderance while left ventricular premature beats occur in the largest proportion of left ventricular preponderance. As this data is based on the relative as well as the absolute proportions of these phenomena it is not unreasonable to suspect an underlying cause. A possible explanation seems to be that the hyperactivity or other abnormal conditions present in that portion of the heart that gives rise to the electrical phenomena of preponderance may likewise cause it to have an increased irritability and therefore more prone to be the seat of origin of ectopic beat formation. The series presented in this study, however, is comparatively small and the difference in relative frequency of right ventricular premature beats in cases showing right and left preponderance so little that one cannot be too cautious in drawing conclusions.

SUMMARY. In a study of 375 cases 36 per cent. showed evidence of left ventricular preponderance and 10 per cent. showed evidence of right ventricular preponderance, while 2 per cent. showed an apparent change in preponderance at different times and under varying conditions.

Premature contractions of all types occurred 76 times in the series of 375 cases (20 per cent.). In the 63 individual cases showing premature beats, 11, or 17 per cent., showed at least 2 different types while 2 cases showed origin in 3 different foci. Left ventricular premature beats were most frequent, right ventricular, auricular and junctional contractions occurring next in order in diminishing frequency.

The greatest percentage of right ventricular preponderance showed right ventricular premature contractions, while the largest percentage of left ventricular preponderance showed ectopic beats arising in the left ventricle. From these facts there is deduced a possible etiological theory to account for the relationship of preponderance and the origin of ectopic beats.

STUDIES IN CHOLELITHIASIS.

III. THE IMMEDIATE EFFECT OF THE VARIOUS TYPES OF OPERATIONS UPON THE CHOLESTERINEMIA.

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AND
MARCUS A. ROTHSCHILD, M.D.
NEW YORK.

(From the Pathological Laboratory of Mount Sinai Hospital.)

IN the second paper of this series it was shown that a proper conception of the underlying pathological disturbance, initiating

disease of the bile passages with stone formation, was only possible in the light of the cholesterin content of the blood after exact knowledge was obtained of actual anatomical conditions. The next stage of the study directed itself, naturally, toward an investigation of the effect which the various types of operation had upon these conditions, especially the effect upon the underlying metabolic disturbance when the latter was present. As a basis for this part of the study there are the variations in the cholesterinemia determined by frequent estimations of the cholesterin content of the blood after operation and the correlation of these with the clinical histories.

It was soon found, however, that in a certain number of the patients the immediate effect differed from the ultimate one observed when the cases were followed over long periods of time. This necessarily complicates matters considerably, and therefore, for a matter of convenience, we have restricted ourselves to giving in this communication only those effects which were seen to follow immediately after operation.

The operations employed at Mount Sinai Hospital are the usual ones made use of in any surgical clinic and given in the order of frequency of their performance are as follows:

1. Cholecystectomy.
2. Cholecystectomy with drainage of the cystic duct.
3. Cholecystectomy with drainage of the hepatic duct through the cystic duct.
4. Cholecystectomy and choledochotomy with drainage of the common bile duct.
5. Cholecystostomy with drainage of the gall-bladder and rarely with choledochotomy and drainage of the common bile duct.
6. Cholecystotomy.

In the classifications hereinafter given we have considered 2 and 3 as accomplishing the same purpose and have therefore grouped them together. The effect of cholecystotomy will not be considered, as we have studies so far in only one case.

These operations were performed on the surgical services of Drs. Lilienthal, Beer, Berg, Elsberg and Moschcowitz, either by themselves or by their associates. We are indebted to all of them for the privilege of carrying on these studies and for their kind coöperation.

In the following tables the variations in the cholesterin content of the blood after each type of operation are given. In each case the interval after operation is noted; also whether any complication such as obstruction had been present.

When estimations are made shortly after this type of operation the variations in the figures are not marked. Many of the differences could be accounted for as being within the limits of personal error. When the observations are made somewhat later, that is at about

the end of tbe second or third weeks, one finds a moderate drop in the amount of blood cholesterin. The decrease has usually averaged about 50 mg. of cholesterin per each 100 c.c. of blood. When the differences are marked there had always been a preëxisting obstruction of the common bile duct which had been relieved by operation.

TABLE I.—CHOLECYSTECTOMY: NO BILE DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.	Remarks.
267	0.125	0.125	13	
284	0.162	0.172	4	
260	0.209	0.125	18	Jaundiced
166	0.190	0.158	14	
181	0.110	0.125	4	
312	0.125	0.1525	6	
306	0.190	0.170	15	
433	0.172	0.162	5	
169	0.155	0.110	15	
382	0.175	0.115	12	
195	0.176	0.162	5	

When the postoperative variation in the cholesterin content of the blood has been a slight rise rather than a diminution we have accounted for the discrepancy in either of two ways: (1) as being within the limit of personal error, or (2) as being due to obstruction in the ducts caused by a temporary inflammatory swelling of the wall structures resulting from the operative trauma.

TABLE II.—CHOLECYSTECTOMY WITH CYSTIC OR HEPATIC DUCT DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
270	0.155	0.140	14
294	0.205	0.195	52
222	0.176	0.162	25
145	0.175	0.172	5

The postoperative variations in the cases in this group are very similar to those in the previous one. Case No. 294 was frequently jaundiced, but this had disappeared a few days prior to operation.

TABLE III.—CHOLECYSTECTOMY WITH COMMON DUCT DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
235	0.190	0.161	14
163	0.235	0.175	7
343	0.242	0.275	6
264	0.200	0.125	24
127	0.237	0.137	6
147	0.212	0.125	15

When the common bile duct is drained the postoperative drop is very marked. In case No. 343 it was noted at the time of operation that there was a marked inflammatory stricture of the common duct secondary to a gangrenous empyema of the gall-bladder. The operative trauma evidently intensified this and accounted for the postoperative increase in the cholesterin content of the blood. Later, when this subsided, the obstruction was relieved spontaneously, and then the cholesterin content of the blood fell to 0.14 mg. per cent.

TABLE IV.—CHOLECYSTOSTOMY WITH GALL-BLADDER DRAINAGE.

Case No.	Preoperative cholesterinemia, mg., per cent.	Postoperative cholesterinemia, mg., per cent.	Days postoperative.
202	0.212	0.185	15
177	0.220	0.1465	10
94	0.150	0.126	8
384	0.207	0.190	5
151	0.215	0.140	6
119	0.237	0.145	8
126	0.200	0.125	6
134	0.290	0.155	7
106	0.2725	0.1665	3
		0.16675	9
177	0.220	0.1415	3
		0.0837	27

These cases show a similarity to those in which a cholecystectomy is performed and the common bile duct is drained. The fall in the cholesterin content of the blood is always large and immediate.

Discussion. The performance of any of these operations immediately produces new conditions which have a variable influence on the metabolic activities of the cholesterin metabolism, and upon its index the cholesterin content of the blood. These conditions may be considered as owing their existence:

1. To the preparation of the patient for operation.
2. To conditions produced by the operation itself.
3. To conditions in the early postoperative period.

More in detail the preparation for operation includes:

1. A short period of starvation.
2. Active catharsis.

The period of food deprivation removes for the time being an important source of intake for the cholesterin content of the body. The active catharsis removes from the bowel the accumulation of cholesterin and cholesterin esters derived from the bile, which, under the usual conditions, would be reabsorbed into the lymphatic system. Both of these combined subserve the same purpose while functioning in diverse ways and accomplish a diminution in the cholesterin content of the body. Inasmuch, however, as these factors are only operative for a short period of time, rarely over twelve to twenty-four hours, the actual result accomplished, as

indicated, in the cholesterin content of the blood is hardly appreciable.

The operative attack necessarily entails:

1. The giving of an anesthesia, usually nitrous oxide gas, followed by ether, very rarely with the addition of small quantities of chloroform.

2. A loss of blood which only exceptionally is large enough to be recognizable in its effects and may therefore be disregarded as inconsequential.

3. A certain degree of insult to the sympathetic nervous system; and in certain instances it accomplishes

4. The drainage of bile from the biliary passages.

The pharmacological action of the various drugs employed as anesthetics is of the depressing variety, and although no special studies have been made upon the effect of these drugs upon the cholesterin metabolism, one may safely assume that this, in common with other metabolic activities, will be diminished. The sympathetic nervous system is intimately connected with the adrenal glands and consequently with the cholesterin metabolism. A disturbance of the normal equilibrium which results from any operative attack will, to a certain degree, be reflected in the changes observed after operation in the cholesterinemia. When a biliary fistula is made the escape of bile diverts from the bowel those cholesterin bodies which normally form one of the important sources of derivation for the cholesterin content of the body. The total effect of all these combined would be indicated in a diminution of the cholesterin content of the blood.

The conditions accompanying the early postoperative period are:

1. The deprivation of food or a diet in which the lipoid content is at a minimum.

2. A short period of constipation which occasionally becomes protracted.

3. The renal congestion consequent to the anesthetic, occurring very frequently, usually lasting only for a few days, but occasionally assuming the characteristics of a true nephritis.

4. The continuation of bile drainage when such a fistula has been established.

The deprivation of lipoid material from the diet naturally lowers the cholesterin content of the body, although it should be remembered that the withholding of all food tends to increase the cholesterin content of the blood. Whenever a biliary fistula is present this diminution in the cholesterin of the body will be all the more enhanced. True nephritides are frequently associated with hypercholesterinemic states of the blood.

With the exception of the question of drainage the factors involved in preparing for operation and those relating to the operation itself

are practically identical for every patient and may be considered as constants. In any discussion therefore these will bear no influence upon the final result. Those factors relating to conditions after operation naturally vary with the individual patient. Of these the most important is the influence of bile drainage.

The escape of bile through a fistula established into the common bile duct is always complete for a variable length of time, but as inflammatory reactions subside a smaller or greater portion of bile will trickle down alongside of the tube into the duodenum. One frequently notices a slight coloring of the stools after a common duct fistula has been draining for some time, whereas, at first, these have been clay-colored. On the other hand the escape of bile through a gall-bladder fistula is complete only when there is associated some obstruction in the common bile duct. The two following cases illustrate this latter point.

CASE No. 106. In a forty-year-old woman attacks of cholecystitis with jaundice had occurred frequently during the previous eighteen months. At the operation a thin, slightly inflamed gall-bladder was found with stones and a cholecystostomy was made. The cholesterin estimations before operation and the changes occurring in the metabolism after operation are demonstrated in the following table:

TABLE V.—CASE NO. 106.

Date.	Blood cholesterin, mg., per cent.	Bile cholesterin, mg., per cent.	Biliuria.	Stool.
Preoperative:				
May 28	0.2725			
June 2	0.250			
Postoperative:				
June 4	....	0.100	None	Colored
5	....	0.100	"	"
6	....	0.075	"	"
7	....	0.067	"	"
8	....	0.134	"	"
10	....	0.120	"	"
11	0.16675	0.108	"	"
12	....	0.102	"	"
13	....	0.092	"	"
15	....	0.089	"	"
16	....	0.079	"	"

CASE No. 177. A fifty-year-old woman gave a history of repeated attacks of cholecystitis in the previous sixteen months without any jaundice. At the operation a thin-walled distended gall-bladder was found containing numerous small facetted stones and a cholecystostomy was done. The cholesterin estimation before operation and the variations occurring in the cholesterin content of the blood and bile after operation are shown in Table VI.

TABLE VI.—CASE NO. 177.

Date.	Blood cholesterin, mg., per cent.	Bile cholesterin, mg., per cent.	Biliuria.	Stool.
Preoperative:				
Sept. 15	0.220			
Postoperative:				
Sept. 24	....	0.091	None	Acholic
25	0.1415	0.085	"	"
26	....	0.0765	"	"
27	....	0.125	"	"
28	....	0.085	"	Colored
29	....	0.110	"	"
30	....	0.106	"	"
Oct. 1	....	0.0905	"	"
3	....	0.094	"	"
5	....	0.116	"	"
8	....	0.0825	"	"
12	0.0837	...	"	"

CASE NO. 106 had no obstruction in the common duct. Relatively small amounts of bile escaped and the stools were well colored. The bile content of cholesterin was relatively within normal limits, indicating that sufficient quantities of cholesterin bodies were being reabsorbed from the intestinal tract to keep up the normal cholesterin content of the bile. The blood cholesterin fell only to the normal level. Case No. 177, for some reason had, immediately following the operation, some inflammatory obstruction in the common duct, as indicated by the clay-colored stools. (There was no bile in the urine and no jaundice, because all of the bile was escaping through the gall-bladder fistula.) The cholesterin content of both blood and bile, and especially the content of the blood, fell far below the normal level, indicating that the body was being depleted of its cholesterin. In both of these cases the food factor was constant, both of the patients being upon the same diet.

The effects of these two means of bile drainage may be summarized as follows:

1. With common-duct drainage the system is rapidly depleted of its cholesterin.

2. Gall-bladder drainage does not accomplish this extreme effect unless there be a concomitant obstruction in the common bile duct.

3. The rate of drop varies and depends upon the initial figure and the length of time of drainage. After a certain minimum is reached there is no further fall in the cholesterin content of the blood.

4. These effects are obtainable only when the operation has been so performed that proper bile drainage is accomplished and all obstructions have been removed from the ducts. This was most perfectly illustrated by the following case:

CASE No. 172. In a twenty-seven-year-old married woman three attacks of gallstone colic had occurred four months, six weeks and four days previous to admission to the hospital; the last two attacks were accompanied by slight degrees of jaundice. The patient was slightly jaundiced at the time of operation. At the operation (September 8) a normal-looking gall-bladder was found to contain small greenish-black stones and the hepatic and common ducts were apparently empty. A cholecystostomy was made. The contents of the gall-bladder were sterile bacteriologically.

On September 12 there was an attack of colic, with slight icterus, which entirely subsided by September 17. On September 26 the notes state that the discharge of bile from the fistula had been profuse, the fluid was turbid and green in color and a stone had been felt in the gall-bladder on the previous day. This was extracted on September 26. Up to October 12 the drainage, however, had continued to be just as profuse, and on the day following the bile passages were explored. A secondary cholecystectomy was done and a stone which was impacted in the papilla was extracted. The hepatic ducts were drained. The character of the bile drainage changed immediately and the color of the bile became clear golden yellow. The convalescence was uneventful thereafter. The cholesterin variations are indicated as follows:

TABLE VII.—CASE NO. 172.

Date.	Temp. ° Fahr.	Blood cholesterin. mg. per ct.	Bile cholesterin.			Biliuria.	Stool.
			C.c.	Sp. gr.	Mg., per cent.		
Preoperative:							
Sept. 6 . .	99.8°	0.155					
Postoperative:					(G. B.)		
Sept. 8 . .	100.0	...	...	...	0.117		
9 . .	101.2	...	190	1010	0.061	None	Acholic
10 . .	100.4	...	140	1010	0.037	"	"
			70	1010	0.054	"	"
11 . .	99.8	...	102	1010	0.0545	"	"
			88	1010	0.051	"	"
13 . .	103.0	...	130	1010	0.0352	"	"
14 . .	102.4	...	192	1010	0.022	"	"
15 . .	100.2	...	122	...	0.0082	"	"
16 . .	100.2	0.162	270	1008	0.031	"	"
17 . .	99.2	...	275	1010	0.0205	"	"
18 . .	99.2	...	470	...	0.0355	"	"
28 . .	101.4	...	450	1010	0.031	"	"
29 . .	99.4	...	530	1010	0.044	Trace	"
Oct. 1 . .	99.0	0.165	...	...	...	None	"
14 . .	101.8	...	111	1012	0.025	"	"
15 . .	101.6	...	110	1010	0.034	"	Slight color
17 . .	99.8	...	...	...	0.066	"	Colored
21 . .	99.6	...	...	...	0.0475	"	Well colored
23 . .	99.6	...	...	...	0.075	"	"
28 . .	99.4	0.125					

While studying this case we were impressed by the fact that the cholesterin content of the blood did not fall after operation to the level, to which ordinarily we were accustomed to see it fall, and we suspected that the bile passages were not absolutely free. It was only after the second operation, when the common bile duct was cleared, that we saw the cholesterin content of the blood fall to the expected low level. In several instances, occurring subsequently, we made use of this principle in making the diagnosis that the ducts had not been thoroughly cleared and were later much gratified to have our diagnoses verified.

The drainage of bile obtained by inserting a tube into the stump of the cystic duct is found practically to be of little effect. It usually happens that such a tube slips out of its proper position and then the drainage corresponds to the leakage which one so frequently sees after the cystic duct has been tied and the ligature has given way. In our experience this drainage is most ineffectual.

When a tube is inserted into one of the hepatic ducts the amount of bile escaping will produce the effects obtained by drainage of the gall-bladder. Our experience would practically lead us to say that it is an inferior method of drainage.

The effect of bile drainage *per se* upon the underlying metabolic activities whose function is the control of the cholesterin content of the body and blood is *nil*. What is accomplished is the removal of that portion of the cholesterin which exceeds the normal minimal content. How thoroughly this is accomplished depends upon the completeness or incompleteness of the biliary fistula, and, when this is complete, one may see the cholesterin content of the blood fall to values below the normal. The depleting effect of bile drainage may be enhanced or retarded by a lack of superabundance of lipoid in the diet, and when a rapid depletion of cholesterin bodies is desirable it is of advantage to submit the patient to a lipoid-free diet.

The loss of bile produced by a biliary fistula has a deleterious effect upon the animal body, and when this has lasted for an appreciable length of time, patients are liable to exhibit any or all of the following symptoms:

1. Disturbance of the digestive function frequently accompanied by vomiting.

2. Greater or less degrees of constipation induced by an absence of bile from the intestinal tract.

3. Depreciation in the general well-being and vigor of the body and a deterioration in the patient's general condition, as evidenced by an impairment in the circulation, in a lessened resistance to bacterial or other trauma and in a general lassitude and muscular weakness.

This deleterious effect may be counteracted or may be forestalled by collecting the biliary drainage and by feeding it after filtration

to the patient by stomach tube. Occasionally one meets with a patient who is able to drink the bile directly, and for this type of patient some of the obnoxiousness may be removed by the addition of salt to the bile.

The operation of cholecystectomy accomplishes two objects: (1) it removes the local focus of infection when that is present, and (2) it removes the reservoir of bile with its contained stones and stagnated bile. The latter removes a part of the end-product of the pathological disturbance in the cholesterin metabolism which has already taken place; the former removes an agent which has complicated this biological disturbance or which has initiated the stone formation. The only permanent effect accomplished is the removal of the infectious process whenever that is present. The effect upon the cholesterin metabolism *per se* is *nil*. The variations which have been seen in the cholesterin content of the blood after cholecystectomy and their proper interpretation may be summarized as follows:

1. In uncomplicated cases the figures do not change appreciably and the variations are within the normal range.

2. When obstruction is present before operation the complete removal of this is followed by a fall from the preoperative hypercholesterinemia, the figures reaching a normal level very promptly.

3. If the preoperative figure has been low because of an associated high temperature the drop of temperature following operation is accompanied by a rise in the cholesterin content of the blood to the normal level.

4. When the postoperative drop has been large and there had been no antecedent obstruction the fall is due to a lipoid-free diet.

The operation of cholecystostomy accomplishes the following objects:

1. It enables one to remove the end-products of disturbed cholesterin metabolism somewhat better than a cholecystectomy without drainage.

2. It affords a surgical method, inferior to cholecystectomy, for draining the infected area. This does not guarantee that the source of infection has been removed and healing may take place before this source has completely disappeared. Recrudescences of infection may therefore be expected and do actually occur. However, there may be occasions when cholecystostomy would yield greater advantage both immediately and perhaps remotely, and when it is certain that no surgical contra-indication exists, such as a strictured or obliterated cystic duct, the procedure should be carried out in preference to cholecystectomy.[1]

[1] It may not be possible to determine this accurately at operation without mobilizing the entire gall-bladder and cystic duct. In any case it depends upon individual judgment.

3. It affords a method of biliary drainage. The competence of this method has been discussed in the earlier part of this paper and the method has been compared with common-duct drainage. The effect of both of these methods of drainage on the metabolic activities was also then discussed.

It becomes increasingly evident, now, that a choice of the proper operation, efficiently carried out, combined with the intelligent use of bile drainage, will restore the individual patient to that condition of life and health when no hypercholesterinemic crisis had yet occurred and when no bacterial infection of the bile passages had yet taken place. It becomes evident, too, that the cause of the hypercholesterinemia has been influenced in no way. More particularly it becomes apparent from this discussion that when the primary factor at fault is infection the better operation is cholecystectomy; that when the primary factor at fault is a disturbance in the cholesterin metabolism the essential thing to accomplish is an adequate and prolonged bile drainage in order to deplete the body of the supersaturation of cholesterin; that when, as happens frequently, both of these causative factors are working hand in hand, both of these factors must be remedied by making use of both of the methods of treatment indicated herewith.

Lastly, from the scientific point of view, it becomes evident that when the proper surgical indication is met it becomes immaterial whether a cholecystectomy or cholecystostomy is done, provided the indications of disturbed metabolism furnished by these blood estimations are met by a prolonged and complete bile drainage.

WAR MEDICINE

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REINFECTION WITH STREPTOCOCCUS HEMOLYTICUS IN LOBAR PNEUMONIA, MEASLES AND SCARLET FEVER AND ITS PREVENTION.

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COLE and MacCallum[1] have reported the results of their study of the bronchopneumonia following measles and certain features of lobar pneumonia reinfection, their work having been conducted in the wards of the Base Hospital, Fort Sam Houston, Texas, the hospital in which I have been working. Their report does not concern itself with the incidence of bronchopneumonia in the whole number

[1] Jour. Am. Med. Assn., No. 16, lxx, 1146.

of measles cases, with many types of reinfection in measles other than bronchopneumonia, with pneumonia following scarlet fever, nor with certain features of reinfection in lobar pneumonia. Nor do they make any recommendations concerning prevention.

As a supplementary report to theirs I purpose to give the incidence of Streptococcus hemolyticus reinfection in lobar pneumonia, measles and scarlet fever as it occurred at the Base Hospital, Fort Sam Houston; to record the mortality of those various conditions, to discuss, largely by means of case histories, their clinical features and to consider methods of prevention in the future. It will be impossible to do so without using very generously the material collected by Cole and MacCallum.

Reports from various army camp hospitals have indicated that there has been a quite universal experience with Streptococcus hemolyticus infection during the past winter. Irons and Marine[2] have reported it from Camp Custer, Michigan, and Hamburger and Mayers,[3] from Camp Zachary Taylor, Kentucky. Irons and Marine's report particularly concerns measles reinfection and Hamburger and Mayer's lobar pneumonia reinfection.

Lobar Pneumonia. From December 1, 1917, to March 1, 1918, there were admitted 319 cases of primary lobar pneumonia; 44, or about 14 per cent. of these, became reinfected with Streptococcus hemolyticus. This does not include a certain very small group of cases in which there was a primary streptococcus infection, affecting particularly the chest. These cases of pneumonia were all originally pneumococcus infections, proved either by sputum cultures, blood cultures, lung puncture or tissue culture at autopsy. Clinically, they looked and acted like lobar pneumonia up to a certain point in the progress of the disease. Hamburger and Mayers seem inclined to the view that many of their cases were primary streptococcus septicemias. We have had very few such cases, and I am sure that our cases were primarily pneumococcus lobar pneumonias and that there is a different explanation for the presence of the Streptococcus hemolyticus. In fact, in one of our cases an endocarditic vegetation gave a pure culture of Type I pneumococcus and the lung tissue gave a pure culture of Streptococcus hemolyticus. Our experience with generalized streptococcus infections was of a different character. Either they followed measles, as Irons and Marine describe, or they were of a much milder character.

The streptococcus infection, then, was grafted upon a lobar pneumonia. In every one of the 44 cases above, bacteriological and clinical evidence, in certain cases, autopsy evidence showed this. The pneumonia epidemic, of which they were a part, was also clinically and bacteriologically a pneumococcus lobar pneumonia epidemic. The streptococcus infection often made itself evident

[2] Jour. Am. Med. Assn., No. 10, lxx, 677. [3] Ibid., No. 13, lxx, 915.

within a very short time. Often a pleural exudate containing streptococci occurred within twenty-four to forty-eight hours after the entrance to the hospital. But in every one of these cases there was an antecedent consolidation, with pneumococci of a type other than Type IV (which might be a normal finding in the mouth) isolated from the sputum or from the blood. I am not here referring to respiratory or thoracic infection following measles, reference to which is made below.

The clinical complications of these cases fell into four general classes: (1) empyema, (2) delayed resolution, (3) lung abscess and (4) localized areas of persistent pulmonary infection.

1. *Empyema.* Empyema was by far the most common of the complications. The following table shows all the empyema complications of the series of 319 lobar pneumonias, with their bacteriology and results:

EMPYEMA.

	Total.	Died.
Fluid showed pneumococcus	22	5
Fluid showed streptococcus hemolyticus	33	17
Fluid showed streptococcus and pneumococcus	1	1
Fluid sterile or undetermined	41	9
Total	97	32

The high incidence and high mortality of the streptococcus infections is at once evident. Over 60 per cent. of the deaths were due to the streptococcus. Add to this the fact that a large number of the cases in Class 4, of undetermined or sterile fluids, undoubtedly were streptococcus and the percentage would go higher. It is interesting to note that the number of pneumococcus empyemata (22) is approximately 6 per cent., a very little higher than the percentage usually reckoned as the average for empyema heretofore in general practice. Lord[4] found 3.8 per cent. in 500 cases.

The clinical features of our cases were similar to those reported by Hamburger and Mayers. The incidence of empyema with us is lower, but can be explained by the fact that they have reported their measles-pneumonia empyemas along with their primary pneumonias. Our series of measles-pneumonia (*vide infra*) showed nearly 90 per cent. having empyema.

Considering the streptococcus empyema alone it was remarkable how frequently the fluid accumulated early in the disease. The fluid was usually far lower in cellular content than the ordinary creamy empyema pus. It was thin, more or less cloudy, brownish and dirty looking. It was not often present in large amounts but was pocketed and quite difficult to discover in many cases. The difficulty of diagnosis and interpretation of physical signs has been mentioned by all observers. The value of the roentgen rays in

[4] Diseases of the Bronchi, Lungs and Pleura.

diagnosis, provided proper interpretation is given the roentgenogram, is very decided.

The cases did not do well either with or without operation. We tried early operation, late operation, aspiration and let-alone policy, with about the same results all through. The cause of death was sepsis in every instance. In many cases we had a positive blood culture. When the cases came to autopsy early there would be found an active or resolving lobar pneumonia in one or more lobes, with patches of interstitial bronchopneumonia scattered throughout usually more than one lobe, both superimposed on the pneumococcus process and in clear lobes, and some combination of pericardial and pleural exudates and peribronchial lymphadenitis. The cases which came to autopsy late after operation showed a very extensive and peculiar process of grayish infiltration throughout the lungs, usually grouped as a cortex about the visceral edge of the pleural cavity. These areas invariably showed hemolytic streptococci. They looked like coalescent multiple alveolar abscesses which had not broken down.

2. *Delayed Resolution.* The second group of cases showed the clinical picture of delayed resolution and comprised 6 cases, with 4 deaths. Delayed resolution, as a diagnosis, requires some comment. One has to defend himself against the suspicion of unrecognized empyema. It will be noticed that the sentence above states that these cases showed the clinical picture of delayed resolution; that is, they showed a lobar pneumonia in which temperature and signs of consolidation, with crepitation, and expectoration persisted for a longer period than was to be expected. It may be stated quite explicitly that they were neither cases of empyema nor miliary tuberculosis. The sputum in these cases showed hemolytic streptococci. The following case from this group will give perhaps the clearest possible idea of its clinical features:

Case I.—Male, aged nineteen years. Entered hospital January 8, 1918. No previous history of measles. There was a lobar pneumonia in the lower lobe of both lungs. Type I pneumococci were found in the sputum. Temperature remained up for fourteen days, respiration and pulse keeping pace.

January 24, the temperature for the first time reached normal. The respiration and pulse were still high.

January 25, the following notes were made: "The patient has apparently had a termination by lysis. He is still very sick: thin and emaciated, with flushed cheeks. He is coughing up thin purulent yellow sputum. There is a dulness, with increased vocal fremitus and abundant sharp, loud, crepitant rales over both sides posteriorly. Aspiration on both sides gives a dry tap."

January 25, leukocytes, 30,000.

January 29, roentgen-ray report: "Cloudiness, diffuse over the base both sides. Diaphragm cannot be seen on the left side."

January 30, examination: "Still coughing up abundant purulent sputum. Physical signs still show dulness and crepitation posteriorly, but the process seems to be clearing."

Bacteriological report on sputum: Contains Streptococcus hemolyticus; no pneumococcus.

February 1, blood culture: Negative.

February 1, roentgen-ray report: Left side clear, diaphragm, now plainly seen; right side still dark, both lungs present a feathery appearance throughout.

February 6, leukocytes, 21,000.

February 6, sputum: Negative for tubercle bacilli.

Clinical improvement was steady from February 1 to February 12. The process in the lung seemed to be clearing up.

February 12, it is recorded that a physical examination of the lungs showed them to be fairly resonant and with only a few spots of crepitation. The roentgen rays on this date showed a few dark spots. On the evening of February 12 his temperature rose suddenly and his pulse rate went from 120 to 150. He became lethargic, finally comatose and died on February 14.

The autopsy showed fresh endocardial vegetations on the aortic valve, from which were cultured pneumococci. There was no fluid found in the pleural cavities. In the lungs there were spots of thickened tissue usually around the bronchi. Those spots were not pustular. Under the microscope they showed a typical interstitial bronchopneumonic process. Lung culture showed Streptococcus hemolyticus.

3. *Lung Abscess.* There was only one case in this group, a lobar pneumonia, with Type I pneumococcus, who began after an interval of eight days after crisis to run a septic temperature, with profuse expectoration of evil-smelling mucilaginous sputum which contained both pneumococci, streptococci and hemolytic streptococci. The roentgen rays showed a diffuse shadow in the right side. Several diagnostic punctures were negative, but at last the needle drew some pus and mucus, along with considerable air, it having entered what felt like a cavity. Operation at this site drained a pus sac, which required entrance through lung tissue and was evidently a lung abscess draining through a bronchus. The patient is making a good recovery.

4. *Localized Area.* There was a final group of cases which can perhaps be explained best by reciting one or two typical clinical histories. There were 4 cases in this group, all mild and all ultimately ending in recovery.

CASE II.—A boy went through a mild lobar pneumonia of short duration. He was well enough to be up and about, but it was noticed that after exertion his temperature chart showed a slight rise. On examination a spot of dulness, over which there were crepitations and increased vocal resonance, was found over the left

posterior lobe, the site of his original pneumonia. His expectoration, which was abundant, showed hemolytic streptococci, although the period of active invasion it had contained Type II pneumococci. The extent of the area of involvement was never bigger than the palm of the hand. It persisted practically without change for seven weeks and then disappeared, quite completely between two weekly examinations.

Case III.—Another case, probably with the same pathology, occurred in a Sergeant in the Medical Corps who had a Type IV lobar pneumonia in the lower lobe of the left lung. He made a good recovery, returned to duty and thirty-four days after the crisis of his original pneumonia he had a sudden sharp pain in the lower part of his right chest. His temperature rose and for four days he was gravely ill. His sputum, which was profuse and purulent, not streaked with blood, on culture showed hemolytic streptococcus. Physical examination showed fine mixed with coarse rales over the lower part of the chest in front; the roentgen rays showed a shadow here just above the diaphragm on the right side, quite sharply limited and no larger than three fingers of a man's hand. The fever in this case terminated by lysis and the physical signs cleared up entirely as well as the roentgen-ray shadow.

It is of interest to note in Case III the length of time which separated the pneumonia from the secondary disease. The physical signs, and especially the roentgen-ray findings, raised the question of abscess.

The cases in this group of mild but persistent pulmonary infection have been quite puzzling. We have had no autopsy, so are in doubt as to the exact pathology. Certain features of a clinical picture as profuse morning expectoration and patches of rales, suggest bronchiectasis. But the localized area of involvement and the favorable termination are against this view and suggest a persisting interstitial bronchopneumonia.

Measles. Between December 1, 1917, and March 1, 1918, there were admitted to the hospital 716 cases of measles. Our statistics are not reliable as to the exact number of complications by streptococcus reinfection in this group, as we have not cultural reports upon all the otitis media, tonsillitis and peritonsillar abscess cases. Many of the cases of otitis media cultured had streptococci present. So also did certain of the tonsillitides, etc. In all there were about 150 cases of otitis. Aside from the ear and throat complications we had 89 cases of bronchopneumonia in this series (12.5 per cent.), 12 cases of articular rheumatism, non-suppurative, 1 case of suppurative arthritis, with general sepsis, and 2 cases of meningitis, with general sepsis. All of these may be ascribed to the Streptococcus hemolyticus. The complications known to be due to the Streptococcus hemolyticus in measles were 97 (14.8 per cent.), and counting those cases above mentioned of otitis media and

tonsillitis in which we have no bacteriological confirmation, but in which the clinical features were identical with those in which we have, the number of complications was over 35 per cent. of the total number of cases.

1. *Bronchopneumonia.* There were 89 cases of bronchopneumonia, of which 42 died (48 per cent.). In every one of these cases Streptococcus hemolyticus was found either in the sputum or in lung-tissue culture. Other organisms (such as the influenza bacillus) were also present, but irregularly. The report of Cole and others upon this group is so complete as to make it unnecessary to do more than summarize briefly the results.

In all the fatal cases fluid was found in the pleural cavity. The fluid always contained streptococci. The physical character of the fluid was similar to the streptococcus cases of empyema following lobar pneumonia, a murky brown, hardly to be designated as pus. In the whole number of bronchopneumonias there were over 80 per cent. of empyemata. Some of these recovered with operations and some with repeated aspirations. I am not able to come to any conclusion as to the best method of treating them.

Besides the bronchopneumonia there were other groups of cases showing a streptococcic origin. These are not mentioned in Cole and MacCallum's report. I record below a series of cases which will give an idea of the varied symptomatology of this group.

CASE IV.—*Measles followed by double otitis media, meningitis, general septicemia and embolic abscesses. Streptococcus hemolyticus found in the blood culture and spinal fluid.*

The patient, a male, aged twenty-five years, entered the hospital December 12, 1917, with a rash over the skin of the chest, neck and face and conjunctivitis and sore-throat. The throat showed a diffuse redness over the pharynx and buccal mucous membrane. Temperature, 101.2 per cent. By December 16 the rash had faded, the temperature was normal and the patient was comfortable.

December 18, he complained of some discomfort in one ear. The temperature was normal. The ear-drums were pronounced normal by the hospital otologist.

December 19, the otologist again saw the patient and reported there was no discernible indication for paracentesis.

December 21, patient was discharged from hospital feeling well, by his own statement, and with a normal temperature for the preceding seven days.

December 22, he had a pain in one ear and consulted a civilian otologist, who performed double paracentesis, with escape of pus from both ears.

December 23, the patient was comfortable, but in the night he became restless and feverish, called his physician, who found he had a temperature of 104°, and removed him to a civilian hospital. The patient did not improve, so that on December 25 I was asked

to see him. His temperature was then 102°, leukocytes, 26,000; both ears draining thick pus.

December 26, he was removed to the Base Hospital at Fort Sam Houston. The next two days he improved slightly, but on December 29 an abscess appeared over the left elbow and another on the left thigh.

December 30, his neck was rigid: lumbar puncture showed a purulent spinal fluid. On smear the spinal fluid showed streptococci and on culture the colonies hemolyzed blood agar. A blood culture taken on December 29 showed similar organisms. Pus from the ear showed a mixed flora, with streptococci present. The patient died on January 3. No autopsy was made.

CASE V.—*Measles, followed after fourteen days by chill, and polyarthritis; suppuration of the right wrist; hemolytic streptococci cultured from the pus from the joint; blood culture positive for hemolytic streptococci.*

January 13, the date of the patient's entry to the hospital, he had a slight temperature. It is also recorded that he had a rash on the chest, abdomen and face, with pharyngitis, Koplik spots and conjunctivitis.

January 28, he had a chill, and a rise in temperature, followed by several other chills, and the next day developed pain in many joints of the body. Only the right wrist remained swollen by February 2. On this date it was incised and free drainage of pus resulted. The pus from the joint showed Streptococcus hemolyticus. Blood culture made on January 31 was reported positive for Streptococcus hemolyticus. Blood culture on March 16 was negative. After running a mild septic temperature he developed an abscess on the left hip which was incised April 1. The course of his disease was slow but showed progressive betterment. On present date he is still alive, progressing favorably and picking up some of the weight that he had lost. The wrist has healed. The blood culture on April 22 was negative.

CASE VI.—*Measles, followed by polyarthritis and bronchopneumonia of slight extent; arthritis favorably influenced by salicylates; Streptococcus hemolyticus found in the sputum; recovery.*

This patient, a male, aged twenty-four years, entered the hospital on January 24, at which time his measles was well advanced. A culture of his throat showed the presence of Streptococcus hemolyticus.

February 5, he had a sudden rise of temperature, and his cough and expectoration, which had been present during his entire stay in the hospital, were increased. Examination of his chest showed no dulness, but a few spots of crepitation scattered throughout the lungs on both sides. This condition progressed favorably, but on February 14 he developed pain and redness around the joints of the elbows, wrists and ankles. None of the joints suppurated, and under salicylates he recovered entirely. The response to the

salicylates was slower than is ordinarily seen in acute articular rheumatism. The chest condition also cleared up, but slowly. Streptococcus hemolyticus was found in the purulent sputum, which he coughed up so abundantly.

CASE VII.—*Measles followed by bronchopneumonia; death sixteen days after entry to hospital; autopsy; lung culture showed Streptococcus hemolyticus.*

The patient, aged twenty years, entered the hospital on January 23, 1918. Symptoms: sore-throat, photophobia, fever and chilliness. Physical examination: conjunctivitis; red pharynx; no tonsillitis. Red crescentic papular eruption over the face and body and cough and expectoration. Diagnosis: measles.

January 28 the fever increased and the sputum was more abundant; it was thin, mucopurulent, greenish gray, but not streaked with blood. The patient was very faintly cyanotic. Quotation from the record February 3: "As he lies in bed a faint duskiness is observable in the face. He is of light complexion, with clear white skin, so that this slight cyanosis is more discernible. There is no flush to his cheek; the eyes are clear; there is no rash on the body. Examination of the chest shows no heart beats; heart sounds are muffled; no murmurs. Right lung in front: no dulness; a few scattered areas of crepitation. The inspiration is twice as long as normal and high-pitched. Left lung in front: resonance good; many large moist rales as well as finer ones. Back not examined this date." From this time on the cyanosis deepened daily, suddenly becoming purplish the day before death. The areas of bronchopneumonia also became larger and more numerous. Death occurred on February 8.

Autopsy showed bilateral lobular pneumonia, confluent on the left side and fibrinopurulent pleuritis on the left side behind. In the left lung the lobules were very distinctly marked out and in the upper lobe on the left side the patches of consolidation were confluent, but distinctly composed of grayish patches clustered about the bronchi. Culture of a piece of lung tissue and culture from the pleural exudate showed hemolytic streptococci.

CASE VIII.—*Measles followed by bronchopneumonia after a period of twelve days; Streptococcus hemolyticus in the sputum; recovery by crisis twenty-six days later.*

This case is recorded as a contrast to Case VII. Case VII was a short, fulminating, rapidly fatal case. Case VIII had a twelve-day period between the decline of the measles and the onset of the pneumonia. During the febrile period cough and expectoration were profuse and the sputum was of the same character as described in Case IV. Physical examination of the chest showed no large areas of dulness but spots of crepitation, especially during inspiration. In contrast to Case IV this patient was never cyanotic. No pleural fluid was discovered. I think it is worth noting that the

febrile period terminated suddenly. This has been noticed in three-quarters of the cases of bronchopneumonia following measles which terminated favorably.

Scarlet Fever. In 134 cases of scarlet fever we have had 7 cases of streptococcus reinfection. Three of these were pneumonias, with 1 death. One of the other cases had fluid in the pleura containing streptococci and recovered by aspiration. The remaining cases of streptococcus reinfections were otitis media. We have been surprised at the mild character of the scarlet fever cases. Compared to the harassing experiences and hideous mortality of measles in an army hospital, scarlet fever, presumably a more serious contagion, has been of very little moment.

Primary Streptococcus Infections. Both the reports of Irons and Marine and Hamburger and Mayers indicate that they have had to do with a large number of primary, usually pneumonic or thoracic, streptococcus infections, We have not seen many of these cases. There have been 2 cases of apparently primary pleural exudate in which the fluid contained this organism and 6 cases of primary bronchopneumonia. They have not been so fatal nor so severe as the secondary infections, 1 death having occurred in the pleural cases and 1 in the pneumonias. It would seem that the original infection, whether measles or lobar pneumonia (to a less extent scarlet fever), gives to this organism a virulence it does not ordinarily have. A. R. Dochez conveyed to me the impression he had that under ordinary circumstances it did not have a very considerable virulence. So far as I have been able to see I am in accord with this view. We have had quite a number of mild cases of bronchitis occurring among the nurses and staff of this hospital in which hemolytic streptococci were isolated from the sputum.

Method of Infection and Prevention. The work of Cole and his associates have left us in no doubt that the streptococcus is spread by carriers in the wards. In one series of studies Lieutenant F. G. Blake found that on culturing all the cases in one measles ward on admission there were 11.4 per cent. of the cases having Streptococcus hemolyticus in the throat. Two days later, on a general culture of the ward, 38.6 per cent. were positive and a few days later 56.8 per cent. were positive. This was done in wards in which the patients were separated by sheets and the attendants masked. The attendants and nurses in these wards did not usually have Streptococcus hemolyticus in their throats; many cultures were taken and only a few positives were obtained. The organism is not, according to competent bacteriologists, a normal inhabitant of the throat. What, then, determines its particular affinity for the lungs of measles and pneumonia cases? That of course we cannot answer, but we can record that the affinity exists. The bronchitis normally accompanying measles acts as a *locus minoris resistentiæ* and as a culture medium for its growth, and apparently the previous

measles has reduced the immunity of the body. It is obvious that the site and the reduced resistance are also present in pneumonia.

The prevention of these reinfections is an immediate question of paramount importance. Certainly, the next draft should be protected from them if possible. Cummings, Spruit and Lynch,[5] in an interesting article, suggest the use of vaccines. Their work has, however, not been carried far enough to admit of conclusions. We have tried spraying the throats of all measles patients with dichloramine-T, but with no appreciable diminution in the pneumonia incidence. In the meantime, and until sufficient cases can be tabulated, there are other and easily instituted means of prevention at our command.

It is very probable that if these soldiers had acquired measles or lobar pneumonia and had been cared for at home—not in contact with other cases—the mortality would have been much lower and the incidence of complications, at least in the measles cases, very small indeed. It has long been a matter of record in the text-books that bronchopneumonia following measles was particularly likely to be frequent in hospital wards where a large number of cases of measles were treated. In this respect we are repeating the experience of the old preantiseptic days with puerperal fever: if the patient were treated by a midwife at home she remained well; if treated in a hospital she became infected.

The procedure which we have now instituted at this hospital is to segregate every case of pneumonia, every case of measles and every case of scarlet fever for a twenty-four-hour period. During this time a swab culture is made of the throat. When it has been determined by the laboratory whether or not the patient is a streptococcus carrier he is delivered to a proper ward. We have designated streptococcus and non-streptococcus wards for lobar pneumonia, measles and scarlet fever. None has been made for German measles, as our experience has led us to believe that German measles is not subject to streptococcus complications. Prior to the determination of the presence of the streptococcus in the patient's throat he should have individual isolation—if possible in a room or a tent by himself; if not, then in a room with as few other patients as possible, separated from them so far as possible, and with the most rigid prevention of contact, by use of screens or sheets between beds. With an adequate number of single rooms in a receiving ward this could be accomplished there, it being the duty of the receiving officer to see that all cases are properly cultured and reported to the proper ward. In addition to this it may be necessary to culture the non-streptococcus wards at various intervals, probably once or twice a week, as there will be some streptococcus carriers not detected on a single throat swab. Separation of beds by sheets is of course still necessary.

[5] Jour. Am. Med. Assn., No. 15, lxx.

The incidence of bronchopneumonia in measles by this method is considerably cut down. It would be unfair to record the statistical results we have had since adopting the plan, as the measles has been diminished and the weather mild, but it promises a working basis for procedure in future epidemics. The result of separating streptococcus carriers with lobar pneumonia has entirely done away with streptococcus reinfections, but here too our results are subject to revision with a more extensive and vigorous epidemic.

A MEMORANDUM ON MILK.

By Dorothy Reed Mendenhall, M.D.,
CHILDREN'S BUREAU, UNITED STATES DEPARTMENT OF LABOR.

An interesting contribution to the question of the control of the price of milk for the use of mothers and young children is given in recent English Acts concerning the "priority" use of milk and the so-called "rate-aided" milk.[1]

The milk-supply scheme for allowing a prior claim on the available supply of milk for expectant and nursing mothers and for children up to the age of five years came into practice in late winter and was disappointing in its results. The families who most needed milk and who fell into the "priority" class were able to buy only a fractional part of the milk to which they were entitled, because they could not afford to pay for more.

The Milk Order (mothers and children) received from the Ministry of Food in March empowered the local authorities to arrange for the supply of food and milk to the "priority" class and to supply this food and milk free or below cost price. This was followed by a Local Government Board Bulletin approving of the order of the Food Controller and enabling local authorities to recover 50 per cent. of the expenditure incurred from the grant for maternity and child welfare.

The problem now facing local authorities, who are sanctioned in subsidizing "priority" milk, is whether to interpret the order on a generous scale, as a public health measure, or to limit the expenditure to only the most necessitous cases. The question of the decision of what constitutes a necessitous case presents another point difficult of solution. It has been proposed either to regulate the giving of milk below cost according to the income of the family relative to

[1] Rate-aided Milk, Maternity and Child Welfare, April, 1918, ii, 135.

the number of children, or according to the amount expended for rent, which would largely obviate personal investigation.

The price of milk in England today is said to be double the pre-war price, though the Government has attempted to put a maximum price on milk, cheese and butter as well as to regulate the sale of these commodities.

The expenditure for "priority" milk in England, either free or below cost, has been made by the Food Controller and the Local Government Board part of the ordinary expense of war. Regret is felt that in the beginning of the war "priority" milk was not kept at the pre-war price and that any deficit was not met by the nation, as in the case of bread.

While our whole country is agitating the subject of the price of milk and schemes for its control, it would seem an opportune moment to consider the possibility of "priority" milk for our mothers and infants as well as the sale of such milk at a pre-war price.

In *The Food Problem*,[2] a book put out with the approval of Mr. Hoover, the milk supply is given as the most indispensable part of the national diet and the element in production that must first be maintained and guaranteed in equitable distribution in order that the nutrition of the people may be maintained under the stress of war conditions. Although bread is here put second in importance to our milk supply the price of bread is controlled in the United States and the price of milk is not.

The Food Administration, the Department of Agriculture and the Children's Bureau of the Department of Labor[3] are united in their effort to make us realize that milk is our most indispensable food. These departments are endeavoring in every way to keep up the production of the dairy herds of the nation and to check the decline in the use of milk that accompanied the rise in price of milk, especially during the last year.

When the three Government services having to do with the production of food, the sale and distribution of food and the protection of maternity, infancy and childhood agree that milk is the article in our diet most vitally affecting the health of our child population, is it not time that national action was taken to ensure the provision of milk for the "priority" class—nursing and expectant mothers and young children?

Several careful studies have been made recently showing the

[2] Kellogg and Taylor: The Food Problem. Macmillan, 1917.

[3] Milk: United States Department of Agriculture and United States Food Administration, United States Leaflet No. 11. The Agriculture Situation for 1918, Part II. Dairying, United States Department of Agriculture, January, 1918. Milk: The Indispensable Food for Children, Children's Bureau, United States Department of Labor.

decline of the use of milk in certain of our large cities.[4] It is probably true everywhere that the consumption of milk has been curtailed as the price of milk has increased, and that as yet the children over two have suffered more than the children under two. People generally have become imbued with the idea that good cows' milk is a vital necessity for infants; on the other hand, the idea is still prevalent that milk for adults and older children is not really "solid food" but a pleasant drink, interchangeable with tea or coffee. In this crisis we dare not trust solely to the gradual education of the public to the appreciation of the fact that milk is the most valuable article in the national diet, the indispensable food for the growing child as well as for the infant and the expectant and the nursing mother. More direct measures are required.

The children of England today are reported to be suffering from deprivation of nitrogenous and fatty foods in the early months of the war. England has shown us in her recent Milk Order what might have helped to prevent this malnutrition in young children. Are we to neglect this warning?

AMERICAN JOURNAL OF CARE FOR CRIPPLES.

Edited by DOUGLAS C. MCMURTRIE. New York, 1917, No. 2, Vol. V.

THIS issue of the *American Journal for the Care of Cripples* is one of the most interesting which have appeared since the province of this journal was enlarged to include the problems of the disabled soldier. The extent to which interest and investigation in this field have grown in this country is well illustrated by the nature of the articles which constitute the present issue. It may be said that it is somewhat characteristic of the progress in this line that the illustrations in this and other journals of the sort have now passed that phase of development of the subject which illustrates the care of the crippled only by means of pictures of artificial hands grasping pitchforks.

It is seen at once, in glancing over this issue, that those responsible for its production have been digging progressively below the surface and have done their part to lay foundations for the great work ahead of us. So many and varied are the articles which make up this number that it is difficult to particularize regarding them.

[4] Milk Prices and the Poor Wage-earner: Weekly Bulletin of the Department of Health, City of New York, November 3, 1917, vol. vi. Studies of the Use of Milk by Families having Little Children: (1) Baltimore, (2) Washington, (3) New Orleans. Children's Bureau, United States Department of Labor.

Among the longest and most important from the stand-point of informatory value to workers in this field are: "Reconstructing the War Cripple in Alberta," by Douglas C. McMurtrie; "Repatriation of the Disabled Soldier in Australia," by Hon. Colonel W. Fitspatrick, C.M.G.; "Vocational Training for the Canadian War Cripple," by Douglas C. McMurtrie.

It is hardly the function of this review to consider in detail the many humanitarian and sociological aspects which form the basis of much written in this field. It is impossible, however, to omit some reference to this phase of the work, and all readers, lay or medical, will value the description given of the work under way in the neighboring province of Alberta. The illustrations of the article are excellent and show, nearly as well as could, a word description, the conditions and nature of the reconstructive efforts. The fact that the men depicted closely resemble our own men adds to the appeal of the article.

A short article of interest, accompanied by four illustrations, is that on the training for war cripples in Paris.

Under "Vocational Training for the Canadian War Cripple" there is presented a live review of many of the fundamental arguments for widespread and organized effort. Because of some ill-founded criticism directed toward the Canadian Commission, appointed for this purpose, it became necessary, in Canada, to appoint a Parliamentary Committee to inquire into the workings of the system, to test the validity of current public criticism and to give the officers of the commission an opportunity to justify the principles on which their work was based.

In the course of this inquiry a great many witnesses were called, and in the recital of their testimony many side-lights are afforded which could not be obtained through simple description of the work. Nearly fifty pages are devoted to questions by the Committee of Inquiry and answers by the witnesses and defendants, which make interesting and profitable reading. Considerable information is adduced as to the purposes of the work and the means of carrying them out, and there are also included specimens of forms and report blanks in use which reflect accurately their scope and detail.

When the problem of reconstruction and the necessity of meeting it presented themselves with insistence before the general public the novelty of the subject took powerful hold of the popular mind, which was at once stimulated to sympathetic interest. As accounts of this work become multiplied, however, it is seen that much of the literature is repetitive and the tendency will undoubtedly exist for many who make but cursory investigation to feel that with a little reading they have well covered the subject.

This will not necessarily follow, however, and when workers in this field are called upon for sustained practical effort much of emotional interest will have to give way to less stimulating but

fundamentally important details. To those workers who will be found active and untiring when the first wave of sympathy has passed the present number of the journal will prove contributory. It is gratifying to observe in the development of the military side of the journal for the care for cripples evidence not only of firm purpose but also of such thorough knowledge, based on investigation, as to ensure results commensurate with the necessity demanding them.

R. P.

PUBLICATIONS OF THE RED CROSS INSTITUTE FOR CRIPPLED AND DISABLED MEN.

Edited by DOUGLAS C. MCMURTRIE. Series I. Issued February 14, 1918. No. 4.

A STATISTICAL CONSIDERATION OF THE NUMBER OF MEN CRIPPLED IN WAR AND DISABLED IN INDUSTRY. BY I. M. RUBINOW.

THIS contribution is of such striking interest and the subject is of so large importance that it seems worth while to quote at some length a few of the tables presented, together with the considerations on which they are based. The first part of Mr. Rubinow's article is devoted to evidence showing that previous statistics and previous war experiences are of little avail as a basis for present discussion. He states that in the past military statistics dealt chiefly with gross numbers only, so far as wounds were concerned, without much analysis of the types presented. He says that no reliable statistics or even estimates could be found as to the number of cripples created by previous wars, and that, furthermore, the numbers engaged at present and the differing conditions would make any such statistics of doubtful value, even if available. The following table shows the proportion of battle losses in various wars caused by rifle, artillery and other agencies, and is taken from figures prepared by Colonel Hunter, of the American War College at Washington, D. C.

Army.	Rifle.	Artillery.	All other.
Union (1861–1865)	90.1	9.8	.1
Prussian (1870–1871)	91.6	8.4	.6
Japanese (1904–1905)	83.5	13.5	3.0
Russian (1904–1905)	84.5	14.5	1.0

It seems that in the present War, according to a statement of General Petain, of the French Army, the losses from artillery are over 35 per cent. for the French and 45 per cent. for the German. On the other hand there has been a tremendous improvement in military medicine and surgery. This may have, however, the rather paradoxical result of increasing the total number of invalids by preventing fatal consequences to many injuries which in the past, under less skilful ministration, resulted in death. It is interesting to note in passing that whereas the number of deaths from disease in the Civil War was more

than twice that resulting from wounds, on the other hand during the first two years of the present War the proportion of deaths from disease was only about 7 per cent. of the whole number. Rubinow gives the following table as a fairly reliable estimate of the killed, wounded and invalids based upon a study made by a Copenhagen Society early in 1917, covering the first two years of the war.

IN THOUSANDS.

	Died.	Wounded.	Total.	Invalids.
CENTRAL POWERS:				
Austria-Hungary	718	1,777	2,495	533
Germany	885	2,116	3,001	635
Bulgaria	25	60	85	18
Turkey	150	350	500	105
	1,778	4,303	6,081	1,291
ALLIED POWERS:				
Belgium	50	110	160	33
France	885	2,115	3,000	634
Great Britain	205	512	717	154
Italy	105	245	350	74
Russia	1,498	3,820	5,318	1,146
Serbia	110	140	250	42
	2,853	6,942	9,795	2,083
Grand total	4,631	11,245	15,876	3,274

Rubinow remarks that, unfortunately, the data of greatest importance, namely, as to the number of invalids, are probably the least trustworthy. They seem to indicate that on an average at least 30 per cent. of the wounded become invalids. Of the total number of wounded in the Union forces of the Civil War, 14.6 per cent. died, of the German forces of the War of 1870–1871, 11 per cent., of the Japanese forces of the War of 1904–1905, 6.6 per cent., and of the Russian forces 3.7 per cent. In the present War the proportion of deaths has been further reduced, as the following table for Germany indicates:

STATISTICS CONCERNING GERMAN WOUNDED.

	Died.	Dismissed from service.	Returned to duty.
August 1914	3.0	12.2	84.8
September 1914	2.7	9.1	88.1
October 1914	2.4	8.7	88.9
November 1914	2.1	10.6	87.3
December 1914	1.7	10.5	87.8
January 1915	1.4	9.9	88.7
February 1915	1.3	10.0	88.6
March 1915	1.6	9.5	88.9
April 1915	1.4	7.4	91.2

Other tables are given, and the writer finally reaches the general conclusion that, given an army of 1,000,000 men operating for a year, some 40,000 may expect to become crippled through injuries to their extremities, requiring placement facilities or vocational reëducation. Following the same line of analysis, with the reservation that caution is necessary in such estimates, the following table is presented, showing the various injuries to be met with under this group.

Amputation of leg	7,100
Amputation of arm	5,800
Amputation of hand	700
Injuries to leg requiring no amputation	9,100
Injuries to arm requiring no amputation	9,500
Injuries to hand requiring partial or no amputation	7,800
	40,000

The last half of the article is devoted to a consideration of the men disabled in industry, together with statistics relating to crippled children in the German Empire. R. P.

REVIEWS

TUMORS OF THE NERVOUS ACUSTICUS AND THE SYNDROME OF THE CEREBELLOPONTILE ANGLE. By HARVEY CUSHING, M.D. Pp. 296; illustrated. Philadelphia and London: W. B. Saunders Company.

THIS book represents a study of tumors of the acoustic nerve. Tumors in the cerebellopontile angle are by no means rare and have been frequently discussed, but this is the first time that tumors of the eighth nerve alone have been so clearly analyzed. The author has probably had a larger surgical experience in this line than anyone else, and of course is competent to speak of them. He begins by an historical review of the literature, the first case having been reported as early as 1830. Cushing has had altogether in his Baltimore and Boston clinics 784 cases of brain tumor, in which 468 have been verified either by operation or autopsy. Of these, 134 were lesions in the posterior fossa, 56 of which were extracerebellar, 30 of the latter arising from the eighth nerve. Then follows case reports of the verified 30 cases. In these the neurological, surgical and pathological data are well presented. Comments follow the presentation of each case.

In Chapter V, Cushing discusses the etiology and incidence of these tumors, and states that acoustic tumors apparently arise from embryonic tissue rests in the peripheral end of the nerve, and their growth may possibly be influenced by such elements as trauma, local infection or pregnancy. A very interesting fact is that the average age on admission of the verified cases was 23.2 years, and he points out that when cerebellar symptoms occur in the first two decades an intracerebellar tumor, more often a glioma, may be suspected. Then follows a discussion of the symptomatology. He summarizes these by stating that "it can be gathered that the symptomatic progress of the average acoustic tumor occurs more or less in the following stages: (1) the auditory and labyrinthine manifestations; (2) the occipitofrontal pains, with suboccipital discomforts; (3) the incoördination and instability of cerebellar origin; (4) the evidences of involvement of adjacent cerebral nerves; (5) the indications of an increase in intracranial tension, with a choked disk and its consequences; (6) dysarthria, dysphagia and finally cerebellar crises and respiratory difficulties."

The discussion of the symptomatology of the eighth nerve tumors is excellent, and where there is so much excellence it might perhaps

be inadvisable to criticise. Nevertheless, it might be well to point out that the discussion of the cerebellar symptoms is not up to date. There is mention of cerebellar ataxia, dysmetria and Babinski's cerebellar hemiasynergy, as if all these were distinctive cerebellar symptoms, whereas all of them are the result of asynergy. It would be well if the term ataxia were not used in association with cerebellar asynergy, for from the reviewer's view-point it should be limited only to such motor phenomena in which there is disturbance of sensation.

In discussing unusual symptoms in eighth nerve tumors, he quotes a number of instances in which pain occurred in the distribution of the fifth nerve, and on page 164 he mentions a case reported by the reviewer. He states: "I feel some doubt, moreover, as to the diagnosis, for one would have expected deafness had the lesion originated from the eighth nerve.' As a matter of fact the tumor grew from the fifth nerve and there was no mention in the paper that it grew from the eighth.

The best part of the work of course is the surgical. In this Dr. Cushing's mastery has been acknowledged for years. The author gives his technic, which is well illustrated. There is on page 278 a table giving a chart of twenty-nine operative cases in the verified series. It shows the instance of the prolongation of life in the operative cases. The table shows that the case mortality has been 20.7; the operative mortality, based on a number of suboccipital operations, 39 in all, has been 15.4 per cent. These are excellent results, and illustrate better than anything else Dr. Cushing's suburb operative ability. T. H. W.

NERVE WOUNDS; SYMPTOMATOLOGY OF PERIPHERAL NERVE LESIONS CAUSED BY WAR WOUNDS. By J. TINEL. Authorized translation by FRED. ROTHWELL, B.A. Pp. 307. New York: William Wood & Co.

THE European War, with all its horrors, has nevertheless been of great scientific value to medicine. Of the different branches of medicine there is none which is likely to gain more than neurology, because of the occurrence of a great number of focal lesions. Already a number of books and papers have appeared on shell shock and on various lesions of the nervous system.

Of discussions on the peripheral nerves the best that has appeared so far is that by Tinel, which is here reviewed. This book was published originally in French in 1917 and an excellent translation was immediately made by Rothwell, after which it was revised

and edited by Cecil A. Joll. The original has a preface by Dejerine, in whose clinic most of the work was done.

Altogether 659 cases were investigated. Of these 408 lesions occurred in the upper limb and 231 in the lower. Of the nerves of the upper limb the musculospiral was injured the most, next following the ulnar, median circumflex and musculocutaneous nerves in order, besides various combinations. Of the lower limbs the trunk of the sciatic nerve suffered most, then the external popliteal nerve, internal popliteal, posterior tibial, long saphenous, anterior crural and so on in order. In other words, practically every peripheral nerve, as well as every cranial nerve, has been injured in this war, and abundant opportunities were furnished the authors to study practically the injury of every nerve in the body.

The book begins with a general survey, the first chapter giving a study of nerve lesions produced in wounds, in which there are excellent illustrations of the various types of nerve sections, tearings, pseudoneuromata, compressions, etc. Then comes a study of the processes of degeneration and regeneration, neuromata, histological lesions caused by nerve wounds and a study of dissociated syndromes and partial lesions. Following this are the methods of clinical examination of a nerve. It is evident that of all of the clinical neurological studies there are none which need more painstaking research than the study of the peripheral nerves, and unless one is equipped by temperament to spend hours in the study of a case a peripheral nerve study had better not be made. Specially careful work must be done, as is shown by the illustrations of the sensory disturbances. It is interesting that only a mention is made of the protopathic, epicritic and deep sensibilities, and that Tinel states that of the ordinary cursory examinations made only the pin method is applied. No further mention is made of Head's work. The clinical types and syndromes are then discussed. The syndromes are those of interruption, compression, irritation and regeneration.

It is interesting that our own S. Weir Mitchell, who first described causalgia in the Civil War, is extensively quoted in this connection. Very unusual cases are cited, especially those of dissociated syndromes. There is an interesting chapter on ascending neuritis, and most interesting are the unusual contractures, brought about in slight lesions of peripheral nerves, a subject which is being developed in this war. Then comes the general diagnosis of peripheral nerve lesions and the specific treatments of the individual nerves, and finally their treatment.

In a word, this is an excellent presentation of peripheral nerve injuries, and shows that a great deal of work must have been done. The illustrations are excellent. No better praise can be given to this book than to say that it carries out the worthy traditions of the Charcot Clinic. T. H. W.

PHYSICAL REMEDIES FOR DISABLED SOLDIERS. By R. FORTESCUE FOX, M.D., Honorary Medical Director of the Red Cross Clinic for Physical Treatment of Disabled Officers. With Chapters by Major R. TAIT MCKENZIE, R.A.M.C., FRANCIS HERMAN-JOHNSON, M.D., and JAMES B. MENNELL, M.A., M.D. Pp. 277; 88 illustrations. New York: William Wood & Co.

A BOOK by so eminent authority as Dr. Fox cannot be other than valuable. The importance of his subject is extremely great and is one that is going to concern the profession in America more and more in the years to come. There will hardly be a community in the whole country that will not have to consider the care of disabled soldiers even long after the discharge from the army hospitals. The establishment of physical clinics will be imperative. Figures published in France show an average reduction in the mass of physical disability of 20 per cent. by properly organized physical clinics, and this has effected an automatic saving to the State in the charge of pensions of nearly two millions sterling per annum.

Dr. Fox's book is essentially a practical one and presents in a convenient form information which is useful in the treatment of soldiers and civilians by heat and cold, in baths, by electricity and radiation, by massage, mechanical apparatus, exercises and medical gymnastics. Major McKenzie's chapter on exercise, giving minute details as to graduation of effort, is especially good. A chapter on the administration of massage, by Dr. Mennell, though short, covers well the indications and results of such treatment in addition to the administration. And Dr. Herman-Johnson, writing on the use of electricity and radiation, describes the advantages and limitations of such aids. Unfortunately the scheme of the book necessitates repetition of text that ought to have been avoided. The many illustrations throughout the volume add materially to its value as a practical guide. C. N. S.

THE MEDICAL CLINICS OF NORTH AMERICA. Boston Number, January, 1918. Philadelphia and London: W. B. Saunders Company.

IT is but necessary to recount the contributors to this volume to prove its interest. From the clinic of Dr. H. A. Christian appears a review of some interesting heart conditions. Dr. Elliott P. Joslin gives a masterly discussion of two cases of severe diabetes. Dr. W. P. Graves writes of his personal views and experiences regarding ovarian organotherapy, referring in detail to indications for the several preparations on the market. From the clinic of Dr. Fritz B. Talbot is a presentation of cases of eczema in childhood, with a

clear-cut discussion of etiological factors. Dr. Harry A. Barnes gives a careful review of Vincent's angina. Dr. John B. Hawes describes the early diagnosis of pulmonary tuberculosis. Dr. Andrew Watson Sellards discusses amebic dysentery and associated conditions. Dr. John Lovett Morse refers to empyema in children, but unfortunately the subject does not permit of much more than a review of long-established facts and gives little opportunity for careful analysis which the author is so capable of making. The same might be said of Dr. Richard M. Smith's discussion of pyelitis in infancy, which, however, is well written and also has the virtue of being to the point.

These and many more make this number of the *Medical Clinics* of universal interest and do credit to the men of Boston.

C. N. S.

LECTURES ON MEDICINE. A HAND-BOOK FOR NURSES. By CHALMERS WATSON, M.D., F.R.C.P.E., Lecturer on Clinical Medicine, Edinburgh University. Pp. 295. New York: William Wood & Co.

THIS is a valuable book on general medicine for nurses, and would serve as an excellent guide for any lecturer to nurses. Its language is not too technical, yet the subjects are covered fully, particularly from the stand-point of nursing care. Answering those critics who may think that the lectures go to some extent beyond the requirements of a nurse, the author states as his opinion that the efficiency of a nurse bears a direct ratio to the knowledge she possesses of the nature of the disease of her patient and to the principles guiding the physician in its treatment.

One of the most useful chapters is the last, which describes in detail the principles of diet. Many unusual and extremely useful recipes are given, which are appetizing even in their written form.

C. N. S.

BURNS AND THEIR TREATMENT, INCLUDING DERMATITIS FROM HIGH EXPLOSIVES. By J. M. MACLEOD, M.A., M.D., F.R.C.P., Physician for Diseases of the Skin, Charing Cross Hospital, Royal Flying Corps Hospitals.

EVERY now and then there appears a book that is truly worthwhile. Such is this handy little volume on burns. The author in the hospitals of the Royal Flying Corps and in the skin department of Charing Cross had a rich field of material upon which to base conclusions. He takes up in well-chosen detail the classification of

burns, the treatment including that of regional burns and the prevention of complications.

There are chapters on burns from electricity; from lightning; from roentgen rays; from radium and from corrosives. The final chapter describes the various forms of dermatitis and internal symptoms due to the handling of high explosives. It is exceedingly interesting. C. N. S.

MINOR MALADIES AND THEIR TREATMENT. By LEONARD WILLIAMS, M.D., Physician to the French Hospital. Fourth edition. New York: William Wood & Co.

To physicians in search for the written experiences of others in the treatment of minor maladies this book will be welcome. It is refreshing in its empiricism, admittedly egotistical and with no uncertainty of diction. It gives the treatment and formulæ that have given the author results in the relief of the symptoms of that great group of a practitioner's patients, namely, those suffering from minor maladies.

There are chapters on colds and coughs, on indigestion, on constipation, diarrhea, vomiting and giddiness, on rheumatism, neuralgia and headache, on goutiness and a very interesting chapter on minor glandular insufficiencies. The author feels that though the microbe—the seed—has ruled the past, the future is with the soil, the endocrine glands.

The book does not permit of much criticism, or rather it admits of so much criticism in its empiricism that it forestalls all criticism. It is, however, well worth while, and the fact that this is the fourth edition proves that it has been a help to many. C. N. S.

PHYSIOLOGICAL CHEMISTRY. By C. J. V. PETTIBONE, PH.D., Assistant Professor of Physiological Chemistry, Medical School, University of Minnesota, Minneapolis. Pp. 328. St. Louis: C. V. Mosby Company.

THE book is essentially elementary in character, and, as the author points out, his aim was to cover the general field of physiological chemistry in such a way as to make students familiar with compounds that are important from a biochemical view-point and with the fundamental processes which go on in the animal body.

Necessarily, therefore, the student is referred to other standard texts for more detailed information. For those who have no need of going deep into the study of the subject this book will be found

about as suitable as could be desired. The first part deals with the theory, while the second part describes the laboratory work. An appendix gives directions for making up quantitative and special reagents. H. D.

SURGICAL CLINICS OF CHICAGO, DECEMBER, 1917. Vol. I, No. 6; Pp. 220; 89 illustrations. Philadelphia and London: W. B. Saunders Company.

THIS number maintains the reputation of this very worthy publication. One is impressed by the selection of cases as well as by the names of those presenting them. They vary widely but maintain throughout the interest of the reader, sometimes because of their importance and infrequency, sometimes because of their importance and frequency, and are of special interest to those surgeons who have not the privilege of the abundant material each contributor to this number possesses. For example, Lewis discusses separation of the epiphysis and T-fractures of the lower end of the femur, myositis ossificans and (with a special discussion on blastomycosis by that authority on the subject, Montgomery) blastomycosis and sporotrichosis. Of special interest are the reports on cancer of the rectum presented by Ochsner, Davis and Bevan. Fourteen surgeons contribute, some on several conditions and all clearly, interestingly and briefly. T. T. T.

INJURIES OF THE FACE AND JAW. By P. MARTINIER, Professor to the Dental School of Paris, and G. LEMERLE, Professor to the Dental School of Paris. Translated by H. LAWSON WHALE, Captain, No. 83, General Hospital, B. E. F. Pp. 345; 168 illustrations. New York: William Wood & Co.

IT is fitting that special attention be given in these days to the repair of injuries of the face and their resulting deformities. The same interest could not have been aroused in surgeons before the war, but most of those now entering the country's service turn to authoritative special treatises on this subject because of their previous unavoidable lack of experience and training. The average physician and surgeon will be first impressed by the amount of work which had been done along these lines even before this war, in which trench-fighting has produced so many and such frightful face injuries. The best work has been done and chief advances have been made by the dental surgeons, who are therefore best qualified to give instruction. This small volume gives most attention to prosthesis or the art of making artificial substitutes for an organ cut off,

two-thirds of it being devoted to this branch of the subject. Although not intended as a technical treatise the methods of treatment and devices which have gained most recognition are explained and largely illustrated. These include the various artificial substitutes for the jaws, larynx, tongue, nose, ears and lips; those which remain exposed to the air and those which remain buried in the tissues. Special chapters are given to fractures of the lower jaw and of the upper jaw, in which is emphasized especially the insufficiency of bandages and slings alone and the value of Cl. Martin's methods of reduction, with troughs sealed by cement, to immobilize when reduction has been accomplished. T. T. T.

Recollections of a New York Surgeon. By Arpad G. Gerster, M.D. Pp. 347; 20 illustrations. New York: Paul B. Hoeber.

In this volume of reminiscences the author follows the main incidents of his life from early childhood in Hungary to the time of his recent retirement from active professional life in New York City. He was born in the little city of Kassa, at the foot of the Carpathians, and he depicts graphically the domestic, educational and political environment in which his first years were passed. Later he studied medicine in Vienna in 1866 to 1872 under Hyrtl and Bruecke, Rokitansky, Skoda and Billroth, when surgical mortality was still appalling. In February, 1873, he first saw a demonstration of the application of the new Listerian method of wound treatment. This was in Volkmann's Clinic at Halle, when the author was on his journey to the United States. First impressions of medical practice in Brooklyn and New York are interestingly described. The opinions he formed of medical students in 1874, and again years later when he took up new teaching duties at the College of Physicians and Surgeons in 1910, are of special interest. This volume of recollections of a busy life will appeal not only to the author's immediate friends and associates but also to a wider circle of readers. W. H. F. A.

Medical Research and Human Welfare. By W. W. Keen, M.D., Emeritus Professor of Surgery, Jefferson Medical College, Philadelphia. Pp. 160. Boston and New York: Houghton, Mifflin Company.

Permeated with the virile enthusiasm of the author, this little book gives us vivid glimpses of the great advances in medicine,

made within the memory of Dr. Keen, now in his fifty-eighth professional year. Interesting references to events occurring when he was a student in Paris or in Virchow's laboratory or to Civil War experiences serve to give one a personal relationship to the events described. The book represents the Colver Lectures of Brown University for 1917, delivered to a general university audience. This mode of presentation demanded a broad, not deep, treatment of the subject, but it has served only to make the book more widely readable and none the less stimulating. It should appeal especially to students of medicine. W. H. F. A.

INFECTION AND RESISTANCE. By HANS ZINSSER, Professor of Bacteriology, College of Physicians and Surgeons, Columbia University; Major, M. R. C., U. S. Army. Second edition. Pp. 585. New York: Macmillan & Co., 1918.

IT was self-evident to those who were familiar with the first edition of Zinsser's *Infection and Resistance* that, with the rapid advancement in the field which it covered and from the excellence of the book itself, a second edition would soon be demanded. In its original form Zinsser's treatise was the first really successful attempt to group and correlate the large mass of important observations and theories that have been collected under the heading of immunology. Previous attempts in English were very inadequate and sketchy, and in no instance compiled by one who had an authoritative and first-hand knowledge of the subject. The extensive monographs in German and French on limited areas of the field, although bibliographically complete, were in most instances of less value from their bias in favor of one or another school of this new science with which their author happened to be identified. An admirable attempt had been made by Emery, some years ago, to give us an outline of the principles of immunity, but his work was rapidly outgrown by increasing knowledge and was also biased in favor of the opsonic school of Wright. There are now several handbooks and laboratory manuals of greater or less excellence in English, some of them elaborately illustrated and most of them accurate in the matter of the experimental details which are used by the laboratory worker in this field. It should be remarked, however, that the advanced worker in bacteriology, who in reality is the only one competent to undertake the practical application of the principles of immunity in diagnosis and therapy, is usually trained in the methods himself and has little need of detailed descriptions of technic, except as he consults them in original articles. It is difficult to see of what value elaborate descriptions of technic can

be to the practising physician who makes constant use of these methods, although he never himself does or should attempt to carry them out with his limited time and experience. What we have all needed, however, both the laboratory worker and the clinician, is a clear-headed, well-balanced discussion of the historical development and present status of the principles of infection and resistance. This is what Zinsser's book has furnished and continues to furnish us with unabated vigor and authority in the second edition. The author himself is an experienced and well-known worker in this field, a contributor as well as a lecturer and applier of the principles which he discusses. Zinsser's presentation of the facts is uniformly marked by a fairness even toward his opponents in those fields with which he is personally familiar. He is among the first in this country to have appreciated the importance of the contributions of the French school of immunity, particularly as exemplified by Bordet, and has never been carried away by the specious argumentation of Ehrlich, as have so many whose knowledge of this field is literary rather than experimental.

The second edition, although keeping in most parts the outline of the first, has benefited and made use of recent advances in the field of immunology. This is notably true in the chapters on anaphylaxis and in those dealing with the practical results of therapeutic immunization in man, where the most recent contributions have been fitted into their proper places and the general summary in each subject thereby to some extent revised. A section on immunity in syphilis has been added and the Abderhalden reaction has been relegated to its proper and less conspicuous place in the general system. The references throughout the book are plentiful and conveniently placed at the foot of the page, and sufficiently ample to lead one to the original sources of information if he so desires. It would be difficult to speak too highly of the scholarly method of this book, its background of first-hand knowledge and its suggestive value in matters of debate, or to overestimate its worth, both to the beginner and the more experienced worker, in this complex and rapidly growing field of medicine. It is a book that should be in the library of every practitioner as well as of every laboratory worker, and it is one which should not be allowed to gather dust on the shelves of him who ministers intelligently to the sick.

F. P. G.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Bile Peritonitis without Evident Perforation of the Biliary Tract.—BUCHANAN (*Surg., Gynec. and Obst.*, 1918, xxvi, 303) says that effusion of bile into the peritoneal cavity has received serious attention only within the last seven years. He reports a typical case, and the results of a study of the literature, from which he concludes that there is no typical disease picture to account for a bile peritonitis without evident perforation of the bile tract. There is a group of recorded cases, with abundant effusion, in which no perforation could be demonstrated at operation or autopsy. These cases may be accounted for in a variety of ways, some fitting one hypothesis and some another, no one theory suiting all cases. The bilious nature of the effusion still lacks the proof of a chemical examination. It is to be hoped that subsequent cases may be subjected to the test for bile acids and bile salts. The cases being so unusual and so atypical the diagnosis has not yet been made even tentatively, the real condition having never been even suspected in any of the published cases. The treatment should be dry mopping of the peritoneal cavity and direct drainage of the common duct.

The Method of New Joint Formation in Arthroplasty.—PHEMISTER and MILLER (*Surg., Gynec. and Obst.*, 1918, xxvi, 406) made an extensive experimental study on dogs and performed three types of operation, the no-flap, pedunculated and free flap, the results being studied and compared. (1) In the no-flap operations: A joint cavity forms which is diminished in size because of more or less obliteration of the recesses about the margins from thickening and ossification of the capsule and adhesions of the synovia. Excised portions of the capsule and synovia are rapidly but atypically restored. Villous synovitis is frequently present even in the oldest experiments. Articular surfaces form on the ends of the bones as follows: over the prominent

portions which contact with and are pressed upon by the opposing bone, a dense bare bony surface forms which as a result of motion soon becomes smooth and shiny; over the sides, grooves and depressed portions, which are subjected to little or no pressure, a fibrous covering forms by outgrowth from the open cancellous spaces along the surface. With increasing age the fibrous covering usually tends to spread over the entire bony surface, gradually absorbing and replacing the dense bare bony areas. This change is a slow one and in some of the oldest and best functionating joints large bony surfaces were present, the process seeming to be at a standstill. The range of motion varies from 50 degrees to almost normal, and generally was greater in the elbow than in the knee. (2) In the pedunculated-flap operations: The flap early undergoes pressure necrosis and disappears except about the margins and along the grooves where it is not pressed upon. As motion is reëstablished, more of the remaining portions are destroyed until eventually little of the flap is left. Only a small part of the base of the flap receives its nutrition through the pedicle. Any other portions which survive become attached to the ends of the bones and participate in the formation of a fibrous articular covering for the region. The changes in the articular surfaces of the ends of the bones are practically identical with those occurring in the no-flap operations. In the regions subjected to pressure a dense polished bony articular surface forms, while in those subjected to little or no pressure a fibrous covering forms partly by outgrowth from the underlying bony surface and partly from surviving remnants of the flap. The size and appearance of the reformed joint cavity and the range of motion were about the same as in the no-flap experiments. (3) In the free-flap operations: The flaps break down and disappear in the same manner and to about the same extent as in the pedunculated flap operations. The changes in the articular surfaces of the bones and the character and mobility of the reconstructed joint are the same as in the other two sets of experiments. Infection, prolonged immobilization, displacement and too extensive and imperfect resection unfavorably influenced all three groups of experiments to about the same degree. *Hence it matters little in experiments on the normal knee and elbow-joints of dogs whether arthroplasty is performed by the no-flap, pedunculated flap or free-flap method. The flaps when used very largely break down and the newly formed joint is about the same, both structurally and functionally, following the three types of operations.*

Arthroplasty with the Aid of Animal Membrane.—Baer (*Am. Jour. Orthop. Surg.*, 1918, xvi, 171) furnishes a further contribution on arthroplasty by the interposition of chromicized pigs' bladder. The object in using a chromicized membrane is to obtain a substance which will remain intact for a long enough period to allow the changes to occur which take place in the construction of the fibrous tissue over the ends of the bones. At the end of the time it should be absorbed, leaving no foreign body, living or dead, within the joint. In this way the joint can approach in character nearest the normal. Such a membrane is found in the chromicized pig's bladder, which has been found experimentally and at second operations on the human subject to remain intact from sixty to one hundred days, a period long enough

to allow a new joint to be made. The greatest possible care in technic is necessary, although there is not the same amount of traumatism or interference with the circulation in the periarticular tissue as is caused by the various flap operations. At the same time the utmost care must be taken in the antiseptic treatment. The author believes that a membrane arthroplasty is the last form of arthroplasty, as no foreign substance remains within the joint. Therefore there is no pain from any remaining interposed living tissue. The operation itself is less extensive than a flap or muscle implantation, and the periarticular tissues are less interfered with. There is no interference with the integrity of a normal part by the removal for a flap of any adjacent structures. Less resection has to be made in order to interpose the intermediary substance. In properly selected cases good, serviceable, painless motion can be obtained by a membrane arthroplasty in most joints, particularly in the jaw and in the hip-joint. In the knee-joints, fibrous ankylosis of the entire joint or bony ankylosis of the femoropatellar articulation gives excellent results by this mode of arthroplasty. In true bony ankylosis of the femorotibial joints the results are still unsatisfactory, but give hope of better results with a better consideration of the difficulties involved.

Fractures of the Skull.—SHARPE (*Med. and Surg. Jour.*, 1918, ii, 319) says that it has become quite a common belief that once a man has had a fracture of the skull and then recovers he is never the same person again. In 1912 he examined the records of three of the large hospitals of New York City during the decade of 1900–1910. The mortality of fractures of the skull was 46 to 48 per cent.; the mortality of the patients operated on was 87 per cent.; this high percentage was due undoubtedly to the operation being postponed until the extreme stages of medullary compression and edema and also to the fact that the operation performed was the "turning down" of a bone flap—a much more formidable procedure than a decompression, and then the bone replaced so that even the benefits of a decompression were prevented. Besides in many cases the dura was not opened, and as the dura is inelastic in adults no adequate relief of the pressure could possibly be obtained. Of the patients, however, who were finally discharged as "well" or "cured" only 34 per cent. could be traced, and of these it was found that 67 per cent. were still suffering from the effects of the injury; that is, two-thirds of them were not as well as before the injury. The chief complaints were persistent headache; a change of personality of the depressed or excitable type, the patient being thus emotionally unstable; early fatigue making any prolonged mental or physical effort impossible, and thus causing inability to work; lapses of memory, spells of dizziness and faintness; and even epileptiform seizures in a small percentage of cases. With few exceptions these cases regained consciousness gradually a few days after the injury and remained in the hospital for periods of four weeks and longer. Their charts made frequent mention of severe headache, a low pulse-rate of 60 or below, signs characteristic of increased intracranial pressure. An ophthalmoscopic examination had rarely been made. Many of these patients still showed the results of the increased intracranial pressure in their fundi and at lumbar puncture. Late decompression gave marked improvement in these cases. The operative findings were always

associated with a "wet," swollen, edematous brain. Sharpe thinks many of the so-called post-traumatic neuroses are superimposed upon this definite organic basis as the result of the brain injury.

The Selection of Abdominal Cases for Operation. — RICHARDS (*British Med. Jour.*, April 27, 1918, p. 471), upon a basis of 200 operations for war injuries, says that the decision as to whether a man wounded in the abdomen should be operated on or not is usually based on the time which has elapsed since the injury and the rate and character of the pulse. Of the patients who survive operation performed in the first twelve hours a high proportion will have had their lives saved by it, and this is true in a lesser degree of those operated on in the second twelve hours. After this time most of those who survive operations are those whose injuries were not originally fatal. Men with a pulse of 120 or over have less than half the chance of survival of men with a lower pulse. Recently wounded men with a rapid pulse should nevertheless be operated on, provided that their condition is as good as it is ever likely to be, that they have a reasonable chance of surviving the actual operation and that the time taken does not prevent the proper treatment of other wounded. Every wound of the abdominal wall, however slight, should be explored, whether signs of internal injury are present or not. If it is found to be penetrating the abdomen should be opened. The necessity for deciding between the claims of abdominal and other cases can be best avoided by good theater organization, the provision of two tables for each surgeon and by not allowing slow operators to do abdominal work. If these measures are insufficient the decision should be left in the hands of the surgeon in charge of the preoperation ward.

A Method of Citrated Blood Transfusion. — ROBERTSON (*British Med. Jour.*, April 27, 1918, p. 477) says that the use of citrated blood for transfusion seems to fill a definite need in that the technic is relatively simple, easily acquired and can be carried out entirely by one medical officer. Furthermore, this method obviates the necessity of having the donor and recipient together, and the blood can be given at the bedside. Stress is laid on the fact that although the technic is apparently simple, certain definite precautions must be observed in the handling of the blood in order to obtain good results. The chief considerations in the technic are to get the blood quickly and cleanly into the citrate, to obtain prompt and thorough mixing of the blood with the citrate and to transfuse the blood so soon as possible after the bleeding. An apparatus is described which can easily be constructed and has been found to work satisfactorily. The blood is received into isotonic sodium citrate, 3.8 per cent. The amount of this solution, 160 c.c., contains 6 grams of sodium citrate, which has no harmful effect. When a good flow is maintained through a needle of adequate caliber and the blood and citrate are well mixed as large a quantity as 800 c.c. of blood may be obtained by this method. A series of 44 citrate transfusions were given under rush conditions at a casualty clearing station, with good results. The immediate effect of the transfused blood and subsequent progress of the cases were fully as good as that seen following ordinary transfusion. No reactions of any consequence were observed.

OBSTETRICS

UNDER THE CHARGE OF

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Two-stage Operation for Carcinoma of the Pregnant Uterus under Paravertebral Anesthesia.—MASON and CONRAD (*Surg., Gynec. and Obst.*, July, 1918) raise the question as to whether it may not be advisable to operate upon pregnant patients having carcinoma in two stages rather than at one time, as is usually done. They describe the following case: The patient, aged twenty-six years, had given birth to one child seven years before, followed by normal recovery. Her previous health had been good. Her last menstruation had occurred about seven months before entering the hospital. She had irregular hemorrhage for three months and pain along the inner surface of the thigh. On examination the patient was poorly nourished, anemic, with hemoglobin index of 55 per cent. The pregnant uterus extended half-way between the umbilicus and ensiform cartilage. On vaginal examination the cervix was hardened, hypertrophied and bled easily upon touch. The patient's condition was so poor that it was thought best no operation should be undertaken; hemorrhage was checked by gauze packing, and the patient was given rest, tonics and forced nourishment until the hemoglobin reached 70 per cent. Sixteen days after entrance to the hospital the patient was given anesthesia by injection from the eighth dorsal to the third lumbar vertebræ and all the sacral segments. The Cesarean operation was performed in sixteen minutes, the abdominal wall remaining relaxed. The baby was ill nourished but cried on delivery, and died six hours later. After the Cesarean operation was completed the cervix was cauterized with the Paquelin cautery and the patient made a good recovery from the operation, but later developed irregular temperature, although the hemoglobin rose to 80 per cent. Twenty-two days after the first operation, under similar anesthesia, the uterus was completely removed. The patient had a very rapid pulse immediately after the operation, but this gradually subsided. In about four weeks after the second operation she left the hospital at her own request. The malignant growth returned and the patient died between four and five months after the first operation. The method of anesthesia employed in this case is of interest: The anesthetic was placed outside the spinal canal about the vertebræ and in close proximity to the nerve trunks as they emerge from the spinal canal through the foramen; each segment is blocked separately, and this is done along the back by using the ribs in the dorsal and transverse processes in the cervical and lumbar regions as guides. A needle the proper length is introduced vertically over the bony landmarks and pushed forward until it meets its resistance; from this fixed point it is not difficult to find the nerve. In the dorsal region the needle is introduced on a level of the spinous process,

about 4 cm. from the medial line, and pushed horizontally inward until the point strikes the rib, then withdrawing the needle nearly to the skin the angle is changed so as to let it pass just underneath the rib and the needle pushed ½ to ¾ cm. deeper. Through the point of the needle lying in the intercostal space, 15 c.c. of 0.5 per cent. solution of novocain, with 1 to $\frac{1}{10\,0\,0}$ adrenalin, is injected. This is repeated on both sides as needed. A somewhat similar proceeding is employed in the sacral region. Before the anesthetic patients are given 10 grains of veronal on the night before the operation and scopolamin and narcophin before the operation. These doses are varied in accordance with the effect desired. Blood-pressure is not much changed and there is little or no depression. The anesthesia continues from two to four hours and then gradually disappears. Patients occasionally have a dry throat which is relieved by taking sips of water.

Blood-pressure in Pregnancy.—DANFORTH (*Am. Jour. Obst.*, June, 1918) gives the result obtained by the study of blood-pressure in 115 private patients and 332 hospital patients. Upon the first series a total of 608 observations were made, the number upon one individual varying from one to seventeen and the age of the patient from twenty-two to forty-three years. The average systolic pressure calculated from the total number of observations is 114, but one patient gave a pressure less than normal, this being 93. There were 24 cases whose ages varied from twenty to forty-three years, and in them the average blood-pressure was 121; the highest pressure was 129. In the hospital cases the pressure reading was done in almost all immediately after delivery. Of those who entered the hospital with pressure below 140 the average pressure on entrance was 119; when the pressure was taken immediately after delivery the average pressure was 116. In all cases when the pressure was 140 or more the history was carefully examined and every effort made by correspondence to find the previous histories of the patient. So far as labor is concerned there is reason to believe that the advent of labor was followed by rise in blood-pressure. From these investigations he concludes that the average blood-pressure of pregnant women is less than that of non-pregnant. In most cases labor causes a rise of arterial tension. The toxemia of pregnancy is accompanied by rise of pressure except in very rare instances, and this rise usually precedes other symptoms.

Two Cases of Extraperitoneal Cesarean Section for Contracted Pelvis.—BROADHEAD (*Am. Jour. Obst.*, 1918) reports two cases of contracted pelvis treated by extraperitoneal section. The first was a negro primipara, aged eighteen years, brought to the hospital in labor. The pelvis was contracted and repeated vaginal examinations had been made. The position and presentation of the fetus was the second with vertex presentation. At operation a suture of plain catgut was passed around the parietal and uterine peritoneum so as to form an enclosed area six inches in length and oblong in outline; incision in the uterus was about five inches long; this was made through the enclosed extraperitoneal layer. After the delivery of the child the uterine cavity was packed with iodoform gauze and the wound sutured with No. 2 chromic catgut. The baby was born in good condition and weighed 9½ pounds. The patient had a high temperature for four

days after operation, then it gradually fell and the patient finally made a good recovery. Eight months later the uterus was suspended or possibly fixed to the abdominal wall. The cervix was closed, firm and high up in the pelvis. The second patient was a primipara who was supposed to have gone over time; to bring on labor an unsuccessful attempt was made to introduce a bag, and a dose of pituitrin was given. The patient was in labor forty-eight hours, having contractions every five to ten minutes, and was examined by five different physicians. On admission to the hospital she was in very poor physical condition: there was feeble uterine contractions and the fetal heart was plainly heard. The extraperitoneal method was chosen because of the many examinations the patient had. Pituitrin was given by hypodermic just before the abdominal wall was incised. As the chorion was opened a foul-smelling, yellowish, purulent fluid escaped freely and was collected for bacteriological examination. The child, a male, weighing $7\frac{5}{8}$ pounds, was delivered without difficulty. Bleeding was moderate, the leukocyte count was 9000 and in spite of the discharge the patient made a good recovery. She was discharged, with the baby, twenty-eight days after her admission. The scar was three inches long, half above and half below the umbilicus. The bacteriological examination of the amniotic fluid showed abundant staphylococci; blood culture done immediately after the operation showed the same germ and some contamination of it. Another case of extraperitoneal Cesarean section was reported by Langrock (*Am. Jour. Obst.*, June, 1918). In his case the indication was contracted pelvis and patient in labor twenty-nine hours before coming to the hospital, during which time she had strong regular pain every five to eight minutes. The membranes ruptured spontaneously at the beginning of labor; the cervix did not dilate. In all the patient had many vaginal examinations. At operation the cut edge of the peritoneum was sutured to the anterior surface of the uterus. One cubic centimeter of pituitrin was given hypodermically and the uterus opened in the midline. The baby and placenta were delivered in the usual way and the bleeding was profuse, but was readily controlled by iodoform packing. The anterior edge of the peritoneum was sutured to the anterior surface of the uterus, leaving an area of the anterior uterine wall exposed. The uterine incision was covered with a continuous suture of plain gut. The final examination of the patient showed the uterus adherent to the anterior abdominal wall over a small area, with the whole of the posterior wall of the uterus, the fundus and a portion of the anterior wall being left to enlarge in a succeeding pregnancy. Mother and child made a good recovery.

Blood Transfusion by the Citrate Method in Bleeding in the Newborn.—Lewisohn (*Am. Jour. Obst.*, June, 1918) reports his experience in 9 cases of newborn infants suffering from hemorrhage and treated by transfusion by the citrate method. By this method it is possible to take the blood from the donor at the patient's home and bring the citrated blood to the hospital for use; 100 c.c. is the quantity usually employed. A superficial arm vein in the elbow region of the baby is exposed by a very small incision. The blood is heated to body temperature by warm water and introduced through a fine cannula. As a rule, bleeding stopped immediately and the patient began to gain strength.

Examination of the record of the 8 cases shows two deaths, one in which the patient went to another hospital after examination. In most of the infants the hemorrhage ceased so soon as treatment was begun.

Postpartum Eclampsia.—CASSELBAUM (*Am. Jour. Obst.*, June, 1918) had an opportunity of observing what is comparatively rare, namely, postpartum eclampsia. The patient was aged twenty-four years and the pregnancy in question was her fourth. Four years previously she had had pain over the region of the gall-bladder, was tender and had slight fever. This subsided under rest, liquid diet and ice-bag. A diagnosis of appendicitis and cholecystitis was made, but no operation was undertaken. In the present instance the patient had given birth to a vigorous female child. Two hours after the birth of the child she had a general convulsion lasting two minutes, and up to the time of her reaching the hospital she had four in all. On admission to the hospital the patient was well nourished and well developed, but in a stupor from which she could not be aroused. There was marked jaundice; the pulse was 80; the heart and lungs were negative. There was tenderness in the right upper quadrant from the costal border to three inches below the ribs. A catheterized specimen of the urine showed a large quantity of albumin, casts, blood cells and bile. During the night following admission she had thirty convulsions and was given veratum viride until the pulse reached 60. After this treatment she had five more convulsions. Three days after admission she became rational, had no more convulsions, but was jaundiced and tender over the gall-bladder. Her recovery was complicated by attacks of mental disturbance and finally by a severe pulmonary edema. She made a tedious recovery.

Interstitial Pregnancy.—STONE (*American Journal of Obstetrics*) reports an interesting case of a multipara, five and one-half months pregnant, with symptoms of intra-abdominal hemorrhage. Upon examination the abdomen was distended by a tumor which appeared movable but was strongly inclined to the right side. It was oval in form and unlike a pregnant uterus. As the patient's condition improved, there was slight delay in operating, and when the abdomen was opened there was a free hemorrhage from a rupture in the upper portion of the tumor. Supravaginal hysterectomy was performed, and on examining the specimen it was found that the blood had come from the thin uterine wall. The pregnancy had been interstitial and the growth of the embryo had greatly thinned the uterine wall and lead to hemorrhage.

Emergency Labors.—CHRISTOPHER publishes (*Jour. Am. Med. Assn.*) his notes on 1300 ambulance cases in New York City. Among these there were 19 cases of labor, 14 of incomplete abortion, and 1 of pernicious nausea of pregnancy. No deliveries were made on ambulance calls. Those patients found to be in labor were taken to the hospital as rapidly as possible. In cases in which the ambulance surgeon found the baby born on his arrival the cord was cut and the patient was given the opportunity of going with her baby to the hospital.

OTOLOGY

UNDER THE CHARGE OF

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Summary of Report on Diseases of the Ear, Nose and Throat in Egypt from 1915.—BARRETT (*Jour. Laryngol., Rhinol. and Otol.*, April, 1918) was instrumental in establishing aural clinics at the Australian General Hospital, in conjunction with the ophthalmic clinic, with the result of the extension of this service throughout the British Expeditionary Forces, it being found that the aural work was heavier than the ophthalmic in the beginning, largely on account of the outbreak of measles among the Australian troops soon after landing in Egypt. The number of cases of aural complication of one kind and another as the result of this epidemic, in addition to cases which were a recurrence of a previous suppurative disease of the middle ear, ran into the thousands, there being also a steady inflow of new cases without predisposition, the result of diseases contracted in the immediate service. Of nearly 1500 cases there were 95 of acute inflammation of the middle ear, 435 cases of chronic middle-ear disturbance of catarrhal origin, 139 cases of concussion deafness and 143 cases of otitis externa. There being generally about 100 cases of measles under treatment, a large number of cases of acute inflammation of the middle ear might be expected as a consequence of the measles, but many occurred without apparent association. The severity of these cases was so unusual that pathological examinations were carefully made, but with few exceptions no other organism than the staphylococcus was found. The cases of otitis externa included furunculosis, of which there was a large number, a cause of deafness quite common in the Egyptian service, with an origin not clearly explainable. There were many complaints of impairment of hearing referred to shell shock. A number of these cases were falsifications, but the considerable number which were genuine presented the unusual symptoms of unilateral deafness due to gun-fire. In some cases the membrane was ruptured, but these were not very numerous. Of the bilateral cases of concussion deafness the majority were hysterical, and these made good recovery when placed on rigid treatment and subjected to faradization of the mastoid region. The difficulty of discriminating between the real and the false cases of deafness is much greater than in the cases of blindness. A number of mis-statements were made and a number of devices were resorted to to detect the fraud. Of these the most successful were the bandaging of the eyes and the testing of the hearing at different distances by unknown sources of sound, the man examined being unaware of the distances at which the noise-producing apparatus was placed and giving answers which revealed malingering by their discrepancy. Furthermore, the soldiers were usually unaware of the nature of the Rinné test by the tuning-fork or of the fact that in middle-

ear deafness a tuning-fork placed on the vertex is not infrequently heard best in the damaged ear or in the ear artificially plugged. By these and other devices it was possible to show that in a certain number of cases the degree of hearing possessed did not correspond with the physical appearance of disease and that it varied from minute to minute. But these cases were very few in number and belonged to what the author calls the "pathological residuum of the army." Within a year the aural service in Egypt was well organized and a large number of clinics had been established, aurists were placed in the principal hospitals and, as time progressed, were placed also in the stationary hospitals, in casualty clearing stations and even in the field ambulances. The functions of these aurists in the base hospitals and on the lines of communication were essentially different, the usual practice being to transfer a man to the base who reports sick with ear, nose or throat disease for the first time unless the case is shown on examination to be a trivial one. A case so referred to the base hospital is thoroughly examined and treated and returned to the front, a full clinical report being sent with him. Such a case cannot be sent to the base a second time unless symptoms have redeveloped and without seeing an aurist in the field ambulance or in the lines of communication. Consequently it was the business of the aurist placed on the lines of communication to treat and return to the front all comparatively unimportant cases and to transmit to the base as speedily as possible anything of importance. Statistics show that the aural cases constitute from 60 to 75 per cent. of the total work of the aurist, nasal, pharyngeal and laryngeal diseases constituting 25 to 30 per cent. The purpose of the aural practice being the production and maintenance of efficient soldiers, the problem became one largely of treatment of otitis media and furunculosis, the method of treatment being thorough, daily cleansing of the external auditory canal and middle ear by the patient by means of a cotton stick, the auricle being drawn upward and backward by the finger tips of the opposing hand and the depth of the canal and the middle ear carefully dry-cleansed in the manner mentioned, this cleansing being followed by the instillation of alcohol, with 6 per cent. of carbolic acid lotion; the fluid being allowed to remain in the ear five minutes and the ear again dry-cleansed and stopped with cotton, each case being obliged to report once a week for inspection of the ear. The result of this simple treatment has been gratifying, and is due partly to the fact that the soldier is accustomed to obey orders and therefore carefully followed directions. In reference to shell-shock deafness the author is in doubt as to its existence, having never seen such a case in his experience in the Egyptian service, although other aurists have reported cases in which the impairment of hearing seemed labyrinthine in its origin.

War Injuries and Neuroses of Otological Interest.—From the seven cases here recorded, JONES-PHILLIPSON (*Jour. Laryngol., Rhinol. and Otol.*, April, 1918) concludes that certain parts of the organ of Corti are frequently more seriously damaged than others and that the labyrinth may be rendered hypo- or hyperexcitable, its normal equilibrium being much altered, it being evident also that a greater effect upon the internal ear is produced through an intact drumhead and one

which stands the force of the explosion; and that the effect is less when the membrana tympani lacerates and is still less in the conditions of previous loss of this membrane. In the author's opinion shell-concussion deafness is due to three factors: (1) cerebral concussion; (2) overstrain, and (3) fatigue of the organ of Corti, the former being due to violent oscillations of the perilymph communicated to the organ of Corti and the latter to continuous violent noises or explosions at close quarters. In temporary or permanent disorganization of the conductive apparatus the prognosis depends on the recovery of these parts. In one class of cases the patient experienced a great shock and was in some instances buried by the proximate shell explosion. He became suddenly deaf and also dumb. In some instances also he had paresis of the arm or leg, or both, the higher centers being here involved. Frequently there was an almost sudden improvement in hearing in a few days as the shock passed off and the disappearance of nervous symptoms generally when the patient was removed from the firing line. In another class of cases a portion of deafness remained to be more or less slowly recovered from by the return of the internal ear to a normal or nearly normal condition. In the third class of cases, including structural damage, there is a more or less permanent imperfection of function—a ruptured membrane, a dislocation of the small bones from one another or the stretching of their attachments to the tympanic wall. These are only slowly recovered from in many instances, but the author is able to quote from cases seen three or four months later and showing a considerable recovery of hearing.

Primary Disease of the Labyrinth as the Result of Focal Infection.—SHAMBAUGH (*American Laryngological, Rhinological and Otological Society*, reported in *Laryngoscope*, January, 1918). The clinical phenomena observed in cases of primary involvement of the internal ear as the result of focal infection were quite definite, although the symptoms varied more or less widely in different cases. The defect in hearing was always quite characteristic. It began as a defect in the upper part of the tone scale, while the hearing at the lower part of the tone scale remained even after the defect for the higher notes had become quite extensive. The loss of hearing might consist of a defect more or less circumscribed in the middle of the tone scale. Paracusis willisiana was never a symptom in these cases, and tinnitus aurium was seldom the annoying symptom which it so frequently was in cases of otosclerosis. In most cases both ears became involved sooner or later, the shortening of bone conduction, in such event, being always present. In one-sided involvement the positive Rinné would be changed to a negative in those cases in which the defect in hearing was quite marked. Symptoms arising from the vestibular part of the internal ear constituted a very important part of the clinical phenomena observed in many of these cases. Primary diseases of the internal ear constituted the most frequent cause of vertigo. Primary degeneration of the vestibular nerve occurred quite independently of a similar process involving the cochlear nerve. In these cases an occasional attack of vertigo was the only symptom indicating disease of the labyrinth. Three distinct types of primary degeneration in the labyrinth might be encountered: (1) where the cochlea alone was involved, producing nerve deafness

and more or less tinnitus; (2) where the vestibule was involved simultaneous with the cochlea, producing, as a rule, occasional attacks of vertigo in addition to symptoms arising from disease of the cochlea; (3) where the vestibular nerve alone was affected and where all symptoms indicating disease of the labyrinth might be absent, except for possible occasional attacks of vertigo. The progress of the disease differed widely in different cases. There might be a gradual increasing degeneration of the parts involved; the progress of the degeneration might be accelerated by acute exacerbations; or the acute attacks might be followed by a long period of quiescence. Primary degeneration of the labyrinth was not infrequently a complication of syphilis, hereditary or acquired. It was also observed as a sequel of the infectious fevers, especially mumps, typhoid, measles and scarlet fever. In a large percentage of cases, however, the etiology was not accounted for. It was in these cases that focal infection was suggested as a possible cause. The similarity between the manner in which the labyrinth involvement took place and the involvement of other nerves in which focal infection was known to be the cause, suggested this conclusion.

Concussion Injury of the Ear.—SHUTER (*Jour. Laryngol., Rhinol. and Otol.*, London, February, 1918) states that he has seen a large number of cases on different fronts, and differentiates between machine gunners and concussion deafness; in the former there are more frequently instances of deafness, in the latter a more general lowering of the whole tone scale, they occur more commonly in cases of preëxisting middle-ear disease, and are due not to acoustic concussion but to the pressure waves caused by a shell explosion, as by the explosion of a German mine in a confined space, in trench cases and after proximate bomb explosions, rendering the patient temporarily unconscious and inappreciative of sound for forty-eight hours. These causes are presented for secondary examination, sometimes months after the injury, with the following combination of symptoms, marked decrease in hearing, by bone conduction, tinnitus, paracusis, better aërial hearing in a quiet room and hearing tones of low pitch aërially better in proportion than tones of high pitch.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Histopathology of Muscle in Gas Gangrene: Contusion, Ischemia and Infection.—RENE SAND (*Ambulance de l'Ocean*) discusses the various pathological changes in the structure of muscles in gas gangrene under the three following heads: (1) lesions due to mechanical cause; (2) lesions due to circulatory disturbances; (3) lesions caused by toxic

infection. In his studies he has endeavored to avoid three very common errors, *i. e.*, he did not restrict himself to cases of gas gangrene but made comparative studies, noting the alterations due to direct compression of muscle as well as those due to gas gangrene. In the matter of technic he advises the use of frozen sections rather than those embedded in paraffin, for he believes that in the latter process the muscle suffers a distortion of its fibers, an effacing of transverse striations with a dissociation of myofibrils. His third care was in the matter of cutting out the blocks for study to avoid disfiguring the form and structure of the muscle elements. Of the 50 cases studied the author never found fatty degeneration or infiltration, amyloid or calcareous deposits in the tissues. Of the lesions produced by shock at a distance, contusion, compression or incision, he found the following changes occurred: (1) interstitial hemorrhages, interstitial ecema and edema of the muscle fibers; (2) loss of transverse striations with greater clearness of longitudinal markings; (3) hyperplasia of the nuclei of the sarcolemma; (4) necrosis of muscle fiber. The majority of these alterations are temporary, not found after fourteen days. In the lesions due to circulatory disturbances, total ischemia, ischemia and lymphatic stasis by compression for several hours and prolonged total ischemia with severing of nerve (Volkmann's disease), he observed characteristic changes. At the beginning there was edema of the muscle fibers, with slight interstitial edema, then total necrosis of the muscle and connective tissue and finally the muscle fiber lost all semblance of structure and became a flaky mass. In the third group we find a study of cases of toxic infection in which the characteristic changes are a hyaline degeneration of the connective tissue and muscle fibers and necrosis and fragmentation of the latter. The typical lesions of gas gangrene are hemolysis, hyaline degeneration and necrosis of connective tissue and muscle fibers. It may be that a preliminary contusion is essential for the development of gas gangrene, but the extension of the lesion is the function of the bacillus; where there is no Bacillus perfringens there is no gangrene. The microörganism becomes embedded in the interstitial tissue; it fastens itself on the muscle fiber and by its toxins produces degeneration and necrosis of the fiber and penetrates farther only when this fiber is in a state of entire disintegration and death. The action of the toxins of Bacillus perfringens, he claims, is incontestable. The reabsorption of the toxic products engendered by the disintegration of muscle brings about certain visceral disturbances, notably nephritis.

Experimental Acute Nephritis.—Goto (*Jour. Exper. Med.*, 1918, xxvii, 413) supplemented an earlier work on experimental uranium nephritis, with further investigations, using cantharidin, arsenic, diphtheria toxin and potassium chromate subcutaneously in the dog. All animals were carefully controlled for at least two days before the poisons were administered. Albumin and casts appeared promptly in the urine of those dogs receiving cantharidin, arsenic and potassium chromate, whereas their appearance in the urine was delayed for two days when diphtheria toxin was used. Histologically, sections of the kidneys of the different dogs showed varying degrees of congestion of the blood-vessels and convoluted tubules, with granular degeneration of the

epithelium of the convoluted tubules as well as granular plugs in the lumina. In addition, the diphtheria toxin produced shrunken glomeruli and a finely granular material in the capsular spaces. Biochemical determinations were carried out on the blood. The results showed a retention of non-protein and urea nitrogen and chlorides, along with a moderate acidosis. These findings were more marked in the cases of diphtheria and chromate nephritis. The author noted from his experiments, however, that the degree of retention of non-protein and urea nitrogen in the blood varied considerably in different dogs receiving the same dose per kilo of a given poison. A second series of investigations was undertaken to ascertain the effect of sodium bicarbonate upon the course of a milder nephritis produced by the same substances. The sodium bicarbonate was given by stomach tube, for several days, at a constant hour each day. The milder degree of nephritis was gained by giving a smaller dose than was employed in the first series, where almost all the dogs died. It was found that sodium bicarbonate, given in this way, diminishes the acidosis, but that, histologically, the grade of nephritis was apparently unchanged. Little or no effect was noted upon the degree of retention of nitrogen and of chloride in the blood.

The Action of Antiseptics on the Toxin of Bacillus Welchii. In the recent studies on the use of antiseptics it has been shown that they are valuable not only in removing bacteria from contaminated wounds, but also in destroying the toxins of the microörganisms. TAYLOR and AUSTIN (*Jour. Exper. Med.*, 1918, xxvii, 375) carried out a series of experiments upon the toxins of the Bacillus Welchii, using pigeons as the indicator for the potency of the toxin-antiseptic mixtures. The toxin was gained by anaërobically growing the microörganisms on special media. The toxin was standardized and then treated with certain antiseptic solutions. The mixture after remaining in contact for five minutes was injected into the pigeon. In this manner it was found that Dakin's solution and chloramine-T will destroy the toxin of Bacillus Welchii. The authors believe that similar destruction of the toxin will occur *in vivo*, as was demonstrated by them *in vitro*. Phenol solutions did not exhibit this effect. Pigeons could be protected against multiple lethal doses of the toxin by the addition of the antiseptic solution.

Cultivation Experiments on the Globoid Bodies of Poliomyelitis.—Owing to the technical difficulties offered in the identification of the globoid bodies isolated from cases of poliomyelitis by Flexner and Noguchi, many investigators have been unable to confirm their results. SMILLIE (*Jour. Exper. Med.*, 1918, xxvii, 319), fully cognizant of the problems involved, has undertaken a simpler and more successful method. Poliomyelitis was produced in rhesus or cynomolgus monkeys by virus inoculated intracranially, intranasally or hematogenously. After the disease had reached its height the animals were etherized and small sterile pieces of cerebrum, cord, liver, spleen, kidney or thymus were put into sterile test-tubes into which a sterile piece of rabbit kidney had been placed. About 15 c.c. of sterile, clear, bile-free, relatively fresh, warm, ascitic fluid of no less than 1015 specific gravity were then added. Complete anaërobiosis was obtained by the hydrogen-

nitrogen jar. As many as twenty-five tubes were placed in each jar and incubated for eleven or twelve days. The second generation was made by taking 0.2 c.c. of fluid from the first and subculturing it in other ascitic-kidney media. In addition 0.1 c.c. was planted in tubes containing a semisolid medium. At least five subsequent generations were made. The same criteria as used by Flexner and Noguchi were employed for the determination of the globoid bodies. In all eighteen monkeys were used. In the first 4 vacuum jars were used and the results were unsatisfactory. The material from 3 other monkeys showed streptococci, which the author regarded as agonal invaders. Of the remaining 11, typical globoid bodies were obtained from 7, with a total of twenty-two strains. The largest number of strains per monkey was six; 2 gave only one strain. Nineteen of the completely isolated strains were obtained from the brain, one from the cervical cord and two from the spleen. Eleven completely isolated cultures were encountered. No positive diagnosis was made unless the globoid bodies were found under at least five different fields. Twenty-eight days was the shortest period of time, after the primary inoculation of the media, which was required for a positive diagnosis, while the longest time was fifty-four days. No definitely positive culture was ever found in the first generation. It was found in another series of experiments that the globoid bodies were unable to attack even the simple sugars. Eight different strains which had been isolated by the author were inoculated into healthy monkeys. Three of the animals exhibited some degree of paralysis after intracranial and intraspinal injection. None of the cultivated strains produced typical poliomyelitis. The author concluded from this that very few cultures retain sufficient pathogenicity to cause poliomyelitic infection in monkeys.

Extracts of Antibodies Obtained from Specific Precipitates of Typhoid-antityphoid Serum Complex.—Recently, evidence has been produced to show that large doses of a bactericidal serum administered for therapeutic effect can and often does give rise to "serum sickness." In order to obtain antibodies in a solution as free from foreign protein as possible, WEINSTEIN (*Jour. Immunology*, 1918, iii, 17) precipitated the antibodies from antityphoid serum by a specific antigen, later dissociating the antigen-antibody complex. The agglutinin content of a highly potent antityphoid serum was used as the indicator of a specific antibody. Owing to the resistance of Bacillus typhosus to autolysis the method of Chickering in making pneumococcus antigen was found to be unsatisfactory. The author obtained the best results by digesting the bacteria in a 2.5 per cent. solution of antiformin, neutralizing with normal HCl, purifying with absolute alcohol and dissolving in normal saline. Equal quantities of such an antigen and antityphoid serum gave the maximum precipitate, which contained, besides precipitins, agglutinins, complement-fixing, bactericidal and protective bodies. The diluted antigens appeared to be more efficacious than the undiluted. By slightly alkalinizing the solution, 5 per cent. of the agglutinins, 50 per cent. of the bactericidal and 60 per cent. of the complement-fixing bodies could be precipitated, whereas strong alkaline solutions promptly destroyed all antibodies. The optimum temperature was 42° C., and there was apparently no advan-

tage in incubating the mixture longer than one hour. Successive washings of the precipitate reduced the agglutinin content. The author was able to confirm the work of Chantemesse and Widal by using simultaneous injections of streptococcus vaccine to increase the virulence of Bacillus typhosus. It was learned that 1 c.c. of the anti-typhoid extract would protect guinea-pigs against a fatal dose of typhoid bouillon culture (2 c.c.) and that 0.2 c.c. of the extract would protect mice against 0.2 c.c. of the culture, also a lethal dose.

Typhoid Bacteremia during the Course of Miliary Tuberculosis.—The accurate differential diagnosis between acute miliary tuberculosis and typhoid fever has long been the bane of the clinician. The occurrence of a typhoid bacteriemia in patients dying of miliary tuberculosis is as interesting as it is unusual. BLOOMFIELD (*Am. Rev. of Tuberculosis*, 1918, ii, 28) reports 2 such cases Both individuals were colored, their ages being eight and twenty-six years respectively. Neither gave a history of typhoid fever. The boy exhibited no clinical evidence of typhoid while the adult showed sufficient signs to be regarded and treated as such. In the youth a pure culture of Bacillus typhosus was obtained from the blood stream on the thirteenth and nineteenth days of his illness, whereas the man showed the same organism in his circulatory system only on the tenth day. Both had a negative Widal reaction. The younger individual developed a meningitis, dying in twelve days; the older was operated upon for a perforated duodenal ulcer twenty-four days after his admission and died ten hours subsequently. At autopsy both cases showed an acute miliary tuberculosis. There were no characteristic lesions of typhoid fever to be found in any organ. The author was inclined to regard both as cases of acute miliary tuberculosis, with an accidental bacteriemia of Bacillus typhosus. He goes on to say that a one-time carrier state would explain the source of the organisms.

A Rapid Method for the Production of Precipitin Antigen from Bacteria: An Attempt to Apply it to the Determination of the Type of Pneumococcus in Sputum.—KRUMWIEDE and NOBLE (*Jour. Immunology*, 1918, iii, 1) propose a method for the rapid production of an antigen from bacteria by dissolving them in antiformin, boiling, neutralizing, extracting with alcohol, diluting with normal saline, centrifuging and decanting. Emphasis is laid on boiling the suspension in antiformin. Antigens were so prepared from broth cultures of pneumococcus and agar cultures of Bacillus typhosus, types of Bacillus paratyphosus, Bacillus diphtheriæ and Bacillus mallei. It was found that unless appropriate dilutions of antigen and sera were employed and the time factor controlled, crossed reactions were numerous and marked, particularly with closely allied organisms. Comparable results, however, were obtained when antigen prepared by the accepted method was used. An attempt to extract a typhoid antigen from the feces was unsuccessful. Antigen was then prepared from pneumonic sputum in accordance with the method above outlined. Equal quantities (0.2 c.c.) of the sputum antigen and type sera were employed and the degree of precipitation recorded. The rapidity of reaction depends, apparently, upon the strength of the antigen. Ordinarily the entire

procedure could be conducted in from one-half to one hour. Positive results were obtained in relatively few cases, although no false reactions were encountered. The authors were impressed by the fact that bacterial antigens are much stronger than serum antigens. They hope to be able to improve the method by future investigations.

Experimental Study of the Pathogenesis of Carcinoma.—YAMAGIWA and ICHIKAWA (*Jour. Can. Res.*, 1918, iii, 1) have undertaken a series of experiments in an attempt to reproduce cancer. Their procedure was to paint a solution of coal-tar upon the surface of the ears of rabbits. By continuing this application over different periods of time, varying grades of epithelial reaction were attained. The authors do not state the exact nature of the coal-tar solution nor the manner of application. Animals were treated every 2 or 3 days for 30 to 360 days. They observed that during the early stages the coal-tar acted as an irritant, inducing a hyperkeratosis. Later, after about 50 days, the hypertrophic epithelium formed elevated and even pedunculated masses. Some of these masses continued to grow after the irritant was withdrawn. As the lesion became still more chronic the epithelial proliferation showed a tendency to downward growth, with invasive qualities. Microscopic examination showed features resembling true carcinomata. They believed that true malignant growth was developed in seven instances, in four of which metastases were found in the regional lymph nodes. The description of the metastases is not clear, and in one case the extension of the new growth is rather assumed than proved. Cancer growth was only obtained in animals which had been treated over a long period of time. In the majority of instances it occurred only after the 150th day. The tissue response to the application of coal-tar differs from the experimental hyperkeratosis induced by means of Sudan III. The coal-tar lesions are primarily pedunculated outgrowths which by the authors are at times spoken of as cutaneous horns. By the procedure of these authors the importance of an irritating agent in the development of new growth is demonstrated.

Acidosis and Acid Excretion in Pneumonia.—PALMER (*Journal of Experimental Medicine*). The study of various urines demonstrates that in the absence of β-hydroxybutyric acid the hydrogen ion concentration and titratable acidity are due largely to the ratio between acid and basic phosphates. Metabolism during the febrile stage of pneumonia results in the production of considerable amounts of acid substances, and the more severe the intoxication the greater the amounts of free organic acid at the hydrogen ion concentration of 5 which are present. There is excreted in the urine of subjects ill with acute lobar pneumonia a large amount of organic acid which is free at a hydrogen ion concentration of 5. The increased ammonia and acid excretion, low carbon dioxide in the blood, diminished affinity of the blood for oxygen and retention of large amounts of alkali indicate an excessive acid production during the febrile stage of the disease. Acidosis as determined by the combined carbon dioxide in the plasma is seldom if ever severe.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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A Note on Weil's Disease (Spirochetosis Icterohemorrhagica) as it Occurred in the Army in Flanders.—STOKES and RYLE report the following: Weil first described this disease in 1886. It was characterized by jaundice, pyrexia, hemorrhages and the fact that it was apparently infectious. Epidemics have been known in the United States, India, Africa, Japan and the near East. During the Gallipoli campaign there was a widespread epidemic of jaundice among the soldiers. As to the etiology of the disease, Inada and Ito, in 1914, reported the discovery of a spirochete in the liver of a guinea-pig which had been injected with the blood of a patient suffering from Weil's disease. These authors found later that the blood of patients recovering from Weil's disease contained protective substances against the spirochete they had found. They also showed that when they injected the blood of patients with Weil's disease during the first five days of the disease into the peritoneum of a guinea-pig the animal developed the symptoms of the disease and they were able to show the spirochete in the liver and blood of the animals in large numbers. The experiments made with normal people and patients with catarrhal jaundice showed no such results. These writers state that as the illness progresses the spirochetes disappear from the blood stream and cannot be demonstrated in the tissues. Weil believed that the infection was through the alimentary canal and Inada supports this view. Ito and Oki, however, have been able to communicate the disease to animals by applying infected material to the uninjured skin, and they therefore think it may be communicated to man by the skin being exposed to infective material. Fifteen cases of Weil's disease have come to the notice of the authors and they have been able to confirm the findings of the discoverers of the pathogenic cause of the disease. In 2 cases they have infected the animals which have shown the characteristic pathological changes and from which it has been possible to demonstrate the spirochetes. With the exception of 1 case all the men at the time of the onset of the disease were or recently had been employed in the trenches. Two of the cases proved fatal. The characteristic symptoms are as follows: The patients have generalized pains in the head and lower limbs, complain of weakness and unsteadiness. Most of them say they have been vomiting and some of them have nosebleed. The onset is accompanied by a temperature of 103° F. On admission the most striking symptoms were the jaundice and the extreme injection of the

conjunctivæ accompanied by great prostration. The authors found, in investigating the symptoms in the alimentary system, that the tongue is very dry, brown and fissured, that all the patients were constipated and vomiting in the early stages occurred in every case. The appetite which was lost during the period of pyrexia, returned as soon as the jaundice began to fade. As to the circulatory system, the pulse rate was, as a rule, slow in proportion to the pyrexia and there was a very definite slowing during convalescence. There was no evidence of respiratory complications. The excretory system was not greatly affected, the only change observed being a slight albuminuria during the pyrexial period in all cases. There were no severe nervous symptoms except in the grave cases. All the cases showed enlargement of the glands. Varying degrees of jaundice were seen. It was usually a lemon or orange tint and the color rapidly decreased as convalescence began. All cases showed an irregular pyrexia and subnormal temperature was common in early convalescence. In summarizing their experimental results the authors say that they had only two positive results among the animals injected with the blood of patients and no positive results were obtained after the sixth day. The infected guinea-pigs became ill between the fifth and seventh days. Their temperature rose to 104° F. and typical pathological changes identical with those described by the Japanese workers were demonstrated by a postmortem examination. Spirochetes were demonstrated in the livers in large numbers. In conclusion, the authors state that they believe the cause of epidemic jaundice in Flanders is identical with that described by the Japanese investigators and that the infective possibilities of the disease should be recognized.

The Etiology of Scarlet Fever.—MAIR (*Journal of Pathology and Bacteriology*) gives a preliminary description of the diplococcus scarlatinæ which he isolated from the throats of scarlet fever patients in 1915. In the present paper he gives a more complete description of this diplococcus with the technic employed for its isolation and identification. He also presents additional evidence in favor of its causal relationship to the disease. The organism can be demonstrated in the throats of scarlet fever patients during the first week of the disease in 87 per cent. of the cases and it disappears, as a rule, from the throat about the fifth week of convalescence. The diplococcus produces in monkeys a disease which in many respects resembles scarlet fever. It is confined to the region of primary invasion. The most outstanding clinical feature of scarlet fever, namely, the rash, has not been reproduced in monkeys.

Further Attempts to Transmit Pellagra to Monkeys.—EDWARD FRANCIS (*Hyg. Lab. Bull. No.* 106) states that the opinion of some workers that pellagra is a specific infectious disease, and the report by Harris, of New Orleans, of the production of pellagra in the monkey by the injection of a Berkefeld filtrate of pellagrous tissues, led the United States Public Health Service as a part of its study of pellagra to attack exhaustively the problem of the infectivity of pellagrous tissues and body fluids for the rhesus monkey. The experiments here reported consist of a series of inoculations and feedings of pella-

grous tissues and fluids into 90 rhesus monkeys, 3 baboons and 1 Java monkey. The experiments here recorded constitute the most exhaustive effort of its kind ever made to infect monkeys from pellagrous tissues. The experiments were begun at the United States Marine Hospital, Savannah, Ga., in July, 1913; were continued through 1914, and were completed in June, 1915. Throughout this period the experimental animals were bountifully fed and were kept under daily observation in cages in a glass-covered conservatory, located on the south side of the hospital and freely exposed to the direct rays of the sun. The sources of the pellagrous material with which the animals were inoculated or fed were 10 autopsies and 50 living pellagrins. In all, 252 experiments were made with material collected during life or at autopsy; in 141 of these, inoculations were made by hypodermic needle; in 82, material was fed by stomach-tube; in 29, feces were applied to the nasal mucosa. With few exceptions each animal was inoculated by more than one route, with two or more kinds of material, from more than one case, and on more than one occasion. Twenty-eight animals were each subjected to a single experiment; 19 were each subjected to two experiments; 17 were subjected to three experiments each; 19 were subjected to four each; 7 were subjected to five each; and 4 were subjected to six experiments each. The material used for inoculation or feeding was disposed of as follows: (*a*) The brain, spinal cord and their membranes were removed at 8 autopsies and injected cerebrally, venously, subcutaneously, muscularly, peritoneally or spinally into 29 rhesus monkeys. (*b*) The buccal, thoracic and abdominal organs except intestines were removed at one autopsy and injected venously or subcutaneously into 10 rhesus monkeys. (*c*) The intestines and fecal contents were removed at 7 autopsies and injected venously, cerebrally or subcutaneously into 18 rhesus monkeys, 2 baboons and 1 Java monkey. (*d*) Skin showing the pellagrous lesions was removed at 5 autopsies and injected cerebrally, venously or subcutaneously into 9 rhesus monkeys and 1 Java monkey. (*e*) Blood drawn from 8 pellagrins was injected venously, spinally, muscularly or peritoneally into 11 rhesus monkeys. (*f*) Cerebrospinal fluid collected at 5 autopsies was injected cerebrally, venously or spinally into 16 rhesus monkeys. (*g*) Spinal fluid collected during life from 28 pellagrins was injected immediately after collection, spinally, into 24 rhesus monkeys. (*h*) Pericardial fluid collected at 1 autopsy was injected venously or spinally into 4 rhesus monkeys. (*i*) Urine from 4 pellagrins giving a marked indican reaction was injected venously into 5 rhesus monkeys. (*j*) Feces from 3 pellagrins with marked diarrhea were after Berkefeld filtration injected peritoneally into 26 rhesus monkeys. (*k*) Feces from 1 autopsy and from 2 living pellagrins were introduced on cotton pledgets into the nasal fossæ of 29 rhesus monkeys. (*l*) Sputum collected fresh each day from 10 spitting pellagrins was fed by stomach-tube to 5 rhesus monkeys. (*m*) The brain, spinal cord and their membranes collected at 2 autopsies were fed by stomach-tube to 25 rhesus monkeys and 2 baboons. (*n*) The entire contents of the buccal and thoracic cavities collected at 2 autopsies were fed by stomach-tube to 16 rhesus monkeys and 3 baboons. (*o*) The entire contents of the abdominal cavity collected at 4 autopsies was fed by stomach-tube to 17 rhesus monkeys and 3

baboons. (*p*) The entire contents of the buccal, thoracic and abdominal cavities were removed at one autopsy, mixed with spoiled corn meal and fed by stomach-tube to 18 rhesus monkeys and 1 baboon. (*q*) Feces collected at 1 autopsy were mixed with spoiled corn meal and fed by stomach-tube to 2 rhesus monkeys. (*r*) Feces collected fresh each day from a fatal case of pellagra with diarrhea were mixed with spoiled corn meal and fed by stomach-tube daily for fifteen days to 6 rhesus monkeys. *Result:* The animals thus experimented upon showed no indications suggesting pellagra nor did they furnish any support for the view that pellagra is an infectious disease.

The Diagnosis of the Enteric Fevers in Inoculated Individuals by the Agglutinin Reaction.—DREYER and WALKER (*London Lancet*) believe that the agglutinin reaction is the most valuable method of diagnosis for the enteric fevers (typhoid, paratyphoid A and B), as the percentage of positive results obtained by culture methods alone does not exceed 50 per cent. In making the tests for agglutinins after inoculation some accurately quantitative method should be substituted for the qualitative methods formerly practised, diagnosis should depend upon a series of several successive observations and the method employed should produce definite and accurate measurements relative to some fixed standard: for instance, the standard agglutinable cultures prepared at Oxford. These methods would do away with the difficulties which arise from the wide practice of inoculation and would help to disprove the statement that protective inoculation against B. typhosus or the paratyphoid bacilli renders the agglutinin reaction less reliable than it is in non-inoculated individuals. The authors state that on the one hand active infection can be diagnosed as well in typhoid-inoculated individuals as in non-inoculated persons; and, on the other hand, the absence of inoculation agglutinins within the first twelve months or more after inoculation is a very rare occurrence in properly inoculated individuals and is no more frequent in the subjects of pyrexial attacks than in persons who remain in perfect health. The writers then attempt to show that the statements and methods of Dr. H. S. Tidy published in connection with a discussion of paratyphoid fever are erroneous. His method of comparison of the number of standard agglutinin units found in normal inoculated individuals with the number found in inoculated persons suffering from paratyphoid fever or other febrile condition is fallacious. His statement that inoculation agglutinins disappear or are diminished as the result of febrile attacks is shown to be disproved as well as his assertion that a serum titer of 100 standard agglutinin units "apparently corresponds to a positive reaction in non-inoculated persons." He claims also that from tables published by Dreyer and Torrens "it is evident that the febrile cases have distinctly less typhoid agglutinin than the normal inoculated persons," but the authors show that he has misinterpreted the data in these tables and has no true evidence to support this claim. Their contradiction of Tidy's statement that inoculation agglutinins disappear or are diminished as the result of febrile attacks is in perfect agreement with the careful work of Grattan, Harvey and Wood on paratyphoid fever in India. These workers showed that in undoubted cases of paratyphoid A fever in typhoid inoculated individuals a marked

increase in the agglutinins for B. typhosus was noted. The question as to whether inoculation agglutinins are diminished after the fourth or fifth day of pyrexia can only be settled by following the serum titer of individuals during the course of an infection by exact quantitative measurements capable of reduction to a constant standard. From the study of a series of cases the writers found that although the typhoid agglutination titer may remain unchanged or only slightly increased during the course of paratyphoid fever, if affected at all, the change produced is one of active rise, either antecedent to or occurring at the same time as the beginning of the rise in paratyphoid B. agglutination titer. In diagnosing mild cases of typhoid and paratyphoid in inoculated persons, of which many occur, a quantitative determination of their agglutinin titer for typhoid and paratyphoid bacilli on three or more successive occasions at a few days' interval should be made before the presence of typhoid or paratyphoid infection can be excluded. In the interpretation of the agglutinin curves it is important to note the exact time of the maximum agglutinin titer, which should occur between the sixteenth and twenty-fourth day of the disease. If there is any deviation from this, careful inquiry should be made as to the accuracy of the dates, and the results should be carefully interpreted.

Anopheles Infectivity Experiments.—MITZMAIN (*Public Health Reports*, September 1, 1916, vol. xxxi, No. 35) states that in 17 experiments in which human beings were employed to test the infectibility of Anopheles punctipennis with Plasmodium vivax, 14 cases of malarial fever resulted. The sporozoites in the mosquitoes used developed ten to twenty-two days after the definite hosts were given an opportunity to bite a patient harboring a scanty number of mature tertian gametocytes. In an attempt to infect several persons with a single specimen of Anopheles punctipennis one mosquito proved to be the sole infective agent in 1 experiment and one proved to be the sole infective agent in 3 experiments. These two specimens when applied to the same person transmitted the infection in 5 cases, while one of them used with a third mosquito succeeded in infecting 4 persons. In these experimental inoculations it was demonstrated that in 9 instances in which two mosquitoes succeeded in transmitting malaria at least one of the pair was proved to be capable of causing the disease when used singly. It was demonstrated in 11 experiments that short exposure to bites was sufficient to cause successful transmission of the disease. In all of the successful inoculations only tertian infection was reproduced. Plasmodium vivax was demonstrated microscopically.

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